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GAS AND AIR IN THE TISSUES: A ROENTGENOLOGICAL STUDY*

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Roentgenologists make use of the shadows cast by the negative density of the air in the air-filled portions of the body in their examinations of those regions. The shadows caused by the accumulation of gas and air in portions of the alimentary canal are also familiar to them. To produce an artificial difference in density for purposes of roentgenographic diagnosis, air and different gases have been introduced into the peritoneal cavity, the cerebral ventricles, the joints and other portions of the body. Following certain injuries, air may be introduced into the soft tissues of the body and gas may develop as a result of infections with gas-producing anaerobic organisms. Such accumulations will cause shadows on x-ray films that, in some cases, may be of the greatest diagnostic importance. Because of the greater number of cases encountered, the value of x-ray examinations in gas-bacillus infection was well recognized in the different army medical corps during the World War, but since then surgeons in civil practice have lost sight of the aid that roentgenology may give them in the diagnosis and treatment of this type of infection.

From the roentgenological viewpoint, Burchard[3] recognizes three types of gas infection: gas abscess, gas phlegmon, and gas gangrene. Morison[7] and Berry[1] divide the cases into localized and diffuse infections or true gangrene. Abscesses or localized infection either rarely occur in civil practice or they are not recognized as such. Burchard, Morison, Berry, and Black[2] describe as an abscess or a localized infection an accumulation of gas around some foreign material, usually a fragment of a projectile, in an infected wound. Such infections may continue for a considerable time, they are not severe, and drainage with the removal of the foreign material usually suffices for a cure. Black reported an interesting series of this type of infection in soldiers wounded in France and transported to England for hospitalization. The patients had received the injury from five to thirty-three days previously. The diagnosis of gas infection in each instance was made by x-ray examination. An escape of gas did not occur at operation, yet the *Bacillus welchii* was obtained from the pus or the foreign body. All the patients recovered.

An infection of this type is described as being characterized by an accumulation of gas around the foreign material, usually in one large bubble, possibly surrounded by several smaller ones, but without an extension into the muscles or other tissues (*Fig. 1*). On x-ray films the gas is clearly shown as a single isolated dark or oval shadow surrounding the foreign body, sometimes with smaller shadows around it. The larger shadow may attain considerable size. Burchard says it is often as large as an apple.

A more common and serious type of gas-bacillus infection is the one classed as a gas phlegmon or as a diffuse type. In this form the organisms gain entrance to the subcutaneous tissues and muscles through any wound that penetrates the skin (*Table 1*). Gas develops as a result of the growth of the bacteria and spreads through the tissues. It accumulates in small bubbles in the subcutaneous tissues and fascia and as layers under the skin, along the

Table 1

INJURIES IN THIS SERIES OF CASES OF GAS-BACILLUS INFECTION

Compound fractures	9
Gunshot injuries	9
Crushing injuries	6
Penetrating wounds	3
Open reductions	2
Lacerated wounds	1
Total	30

*Read in Section on Radiology, Southern Medical Association, Twenty-Fourth Annual Meeting, Louisville, Kentucky, November 11-14, 1930.

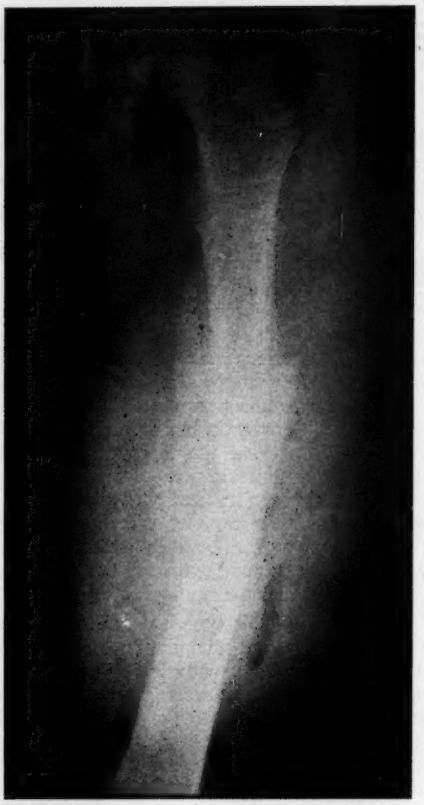

Fig. 1

Possible gas abscess. An oblique fracture of the thigh was operated upon and a metal band applied. The wound became infected and all but a small part of the band was removed. Note the elongated shadow of gas or air parallel with the femur. A laboratory examination was not made.

muscle sheaths, and the intermuscular septa. An extremity is involved with the gas having a longitudinal distribution both proximal and distal to the wound.

The gas in this type of infection has a characteristic appearance on x-ray films. The small bubbles cause round, oval, or elongated shadows arranged in rows or presenting a reticular appearance. The layers of gas will be shown as dark streaks on the images of those portions of the part through which the rays have passed tangentially to reach the film. The size of the shadows and the thickness of the streaks will depend on the amount of gas present, which in turn is proportional to the severity and duration of the infection.

When true gangrene has occurred, the infection has extended into the substance of the muscles, causing necrosis. The gas may replace the

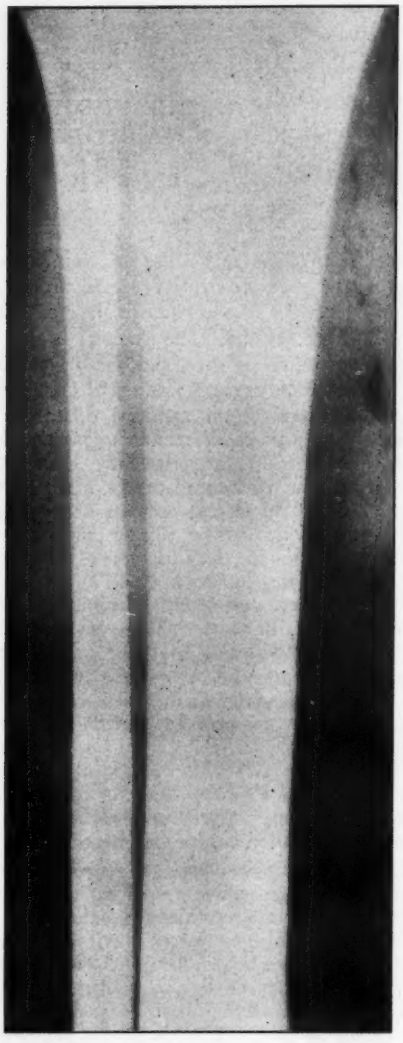

Fig. 2

Localized gas bacillus infection along the tract of a pistol bullet wound of the calf. This film was made eight hours after the injury. Incisions, irrigations and large doses of immune serum resulted in recovery without loss of function.

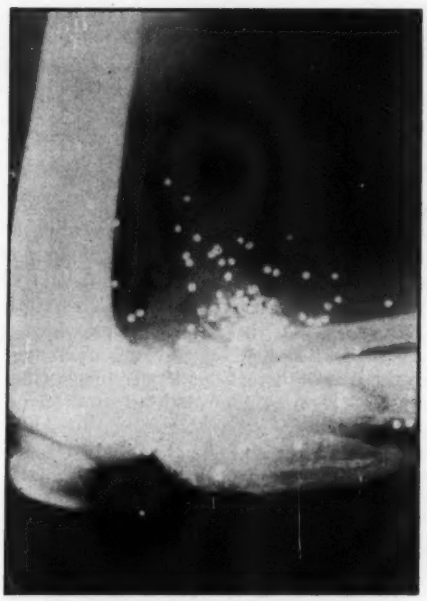

Fig. 3

Gas gangrene following a gunshot injury of the popliteal space. The roentgenogram was made nine and a half hours after the injury. The x-ray diagnosis was disregarded. The condition was clinically apparent at the end of forty-eight hours. Amputation through the middle third of the thigh did not save the patient.

muscle substance and be present with a sponge-like arrangement of the bubbles, or it may accumulate between the bundles of muscle fibers. In the former a definite reticular appearance is present as shown by the shadows on x-ray films. In the latter the direction of the muscle fibers can be seen by the feathery arrangement of the streaks of gas. If more than one muscle be involved with the muscle fibers arranged in different directions, the muscles are well outlined and shown by the shadows of the gas in them. Patients with true gas gangrene either succumb or an amputation is imperative as a life-saving procedure (*Figs. 3* and *4*).

To prevent mutilating operations and loss of life, early diagnosis and immediate treatment are essential in the more severe forms of gas-bacillus infection. Firor[3] makes the statement that in the early period of these infections the presence of gas cannot be detected. He says that in a few cases an early positive diagnosis may be made by x-ray examination. Weintrob and Messeloff[11] give the incubation period of the infection as three days and recommend early and repeated x-ray examinations in doubtful or suspicious cases. Morgan and Valvendre[6] found that a diagnosis could be made earlier by means of x-ray than by any other method. Strauss,[10] by means of experimental infections in guinea

Fig. 4

Gas gangrene from a crushing injury of the lateral aspect of the ankle. The x-ray was made ten hours after the injury. The diagnosis was made by means of x-ray examination. In spite of amputation the patient died. Note the outlining of the muscles by the gas.

pigs, found that gas would be shown on roentgenograms in four hours after the injection, and a more rapid gas production if the circulation had been interfered with by tying the artery. Savill[8] reported that wounded soldiers examined and treated within twenty-four hours of the receipt of the injury were soon convalescent, but those wounded for three or four days either succumbed or required amputations for relief. Sprague[9] says that gas can be recognized within twelve hours after the entrance of a foreign body, a statement in which Welch concurs.

The earliest symptoms of gas infection probably are pain out of proportion to the severity of the injury and a serosanguinous discharge. Marked swelling, the formation of blebs, discoloration of the skin, high temperature, rapid pulse, crepitus, and a foul odor, those making up the classical picture of gas gangrene, are all symptoms of a well-established infection. In our series of 30 cases of gas infection, 17 had x-ray examinations of each injury, 16 of which showed the presence of gas. The films of one patient, taken one and a quarter hours after the injury, were negative. Of the 16 positive films, the longest time after the injury was seventy-two hours, the shortest two and a half hours, and the average twenty and a half hours (*Table 2*).

Table 2

Patients examined by x-ray	17	
Showing gas	16	
Not showing gas	1	
Longest time after injury	72.0	hrs.
Shortest time	2.5	hrs.
Average time	20.5	hrs.

In 11 of these 16 cases the diagnosis was made by finding the shadows of the gas on the x-ray films. The longest durations after the injury were 72 and 50 hours, but both of these patients had been operated upon between the time of the injury and the first x-ray examination. The average time for the x-ray diagnoses was 18.8 hours. If the two cases listed above are not included, the average time after the accident for the x-ray films of the other 9 patients to be positive for the presence of gas was 9.5 hours (*Table 3*).

In 19 of the series, the diagnosis was made from the clinical picture. The shortest time after the accident was twelve hours, the longest 75 hours, the average being 50.5 hours (*Table 3*). Comparing the average time for clinical symptoms to be sufficient to make a diagnosis and that for the appearance of the characteristic shadows on the x-ray films, there is an average margin of 30 hours in favor of the x-ray examinations. In such a rapidly spreading and serious condition as gas-bacillus infection, the average margin of 30 hours might have a decided influence on the prognosis. This is true in this series. Of the 19 patients on whom the diagnosis was made clinically, 10 died and 9 recovered; of the 11 patients diagnosed by means of x-ray, 2 died and 9 recovered (*Table 4*).

Table 3

Diagnosis clinically	19	
Shortest time	12.0	hrs.
Longest time	75.0	hrs.
Average	50.5	hrs.
One omitted 14 days		
Diagnosis by x-ray	11	
Shortest time	2.5	hrs.
Longest time	72.0	hrs.
Average	18.8	hrs.
Average, omitting 2	9.5	hrs.

Table 4

Number of patients	30
Diagnoses clinically	19
Died	10
Recovered	9
Diagnoses by x-ray	11
Died	2
Recovered	9

The x-ray examination of cases of gas infection is important also as an aid in the selection of the proper treatment. The location of the infection in the subcutaneous or muscular tissues, its depth in an extremity, its longitudinal extent, and the amount of tissue destruction can be determined. From these an intelligent opinion can be formed as to whether the treatment should be conservative or radical. If conservative, the location of the incisions and the placement of the irrigating tubes can be controlled so that the treatment will be directed to the infected regions. If gangrene has progressed so that radical treatment is indicated, the extent of the destruction can be determined and the proper level for amputation chosen. In early and limited infections, proper incisions and irrigation, with the administration of large doses of immune serum, may have such prompt results that, if the pathologist's swab cultures do not develop enough gas to blow the stoppers out of the tubes, the surgeons may doubt the correctness of the diagnosis.

The soft tissues in compound fractures, crushing and lacerating injuries, penetrating wounds, and gunshot injuries, either by pistol or shotgun, the same injuries that may be complicated by gas infection, may contain sufficient air to cast shadows on roentgenograms. The air is around the ends of the fractured bones in com-

pound fractures. It probably is sucked into the soft tissues when the ends of the bone are pulled back into the flesh. In the other injuries it is carried into the tissues by the violence that causes the trauma. In all these, the air has a distribution only within the region of the injury and not extending into the surrounding tissues.

Air may spread, however, to a considerable distance in cases of surgical emphysema. In this condition the lung must be punctured and there must be a tract from the subcutaneous tissues of the chest or neck through the visceral and parietal layers of the pleura into the pleural space or lung. Air in the soft tissues from a punctured lung may extend over a wide area of the body, even reaching from the scalp to the middle of the thighs. The appearance on x-ray films of the air of a surgical emphysema is the same as that of the gas in the more advanced gas infections. A report of one case of both conditions has been found.

In one other condition radiolucent shadows may be found in the soft tissues remote from the site of an injury. When a wound has been irrigated or cleansed with hydrogen peroxide, the liberated oxygen may develop sufficient pressure to force its way into the surrounding structures for a considerable distance. As an experiment we irrigated the tract of a bullet through the calf of the leg with peroxide. A roentgenogram made immediately afterward showed a wide distribution of the liberated oxygen. The appearance on the film was indistinguishable from that of an early gas infection. Unless constantly replenished, as in surgical emphysema, air and oxygen in the soft tissues usually will disappear in a few hours. Should there be doubt as to the cause of the radiolucent shadows on the films of an injured region, a re-examination after a few hours should be decisive, for air will decrease or disappear and gas will increase in amount. The importance of re-examination is emphasized by Sprague, who says that a second plate, taken six hours after the first, will show a definite progression in gas infection.

The kind of roentgenograms that are made in the examination of an injury may have some bearing on the early detection of gas infection. Films showing some detail in the soft tissues are required. In compound fractures and gunshot injuries, for example, it is possible to over-expose the films and blot out the shadows of the soft tissues to such an extent that gas will not be apparent, yet the bones and metallic foreign bodies be shown with diagnostic detail. The soft tissues around an injury, if the least over-exposed, should be examined with transmitted light considerably stronger than the usual illuminator. In case of doubt, here again a second exposure, particularly to show the soft tissues, is advisable.

It is possible also to expose a single film in such a manner that gas may not show. Experimentally we have found that as small a quantity of air as 1 c. c., if injected under the skin or into the muscle, will cast a characteristic shadow on a properly exposed film. The air under the skin spreads out in a thin layer that causes a black streak when examined by rays that pass transversely through this layer to reach the film. In the muscles the air causes an irregular black shadow that soon spreads through the muscular tissue. In both instances the air rapidly disappears. Usually one of the two requisite exposures of an injury, made as nearly as possible at right angles to each other, will show the region of the injury in such manner that if gas be present its shadows will be detailed on the film.

By way of conclusion permit me to refer to the statement made by Christopher[4] that x-ray films made of any type of injury in which the skin is damaged or broken, including the open reduction of fractures, if made within ten days of the injury, should be carefully examined for the shadows of gas. In this way the diagnosis of gas infection will be made sufficiently early to permit conservative teatment and the saving of life and limb.

CONCLUSIONS

(1) Roentgenologically, infections with gas-producing organisms appear in the form of gas abscesses, gas phlegmons, and gas gangrene. Each form shows a characteristic appearance on roentgenograms.

(2) The diagnosis of gas-bacillus infection can be made, on the average, earlier by means of x-ray examination than by any other method.

(3) The location and extent of gas infection as shown on x-ray films is a distinct aid in the selection of the proper form of treatment.

(4) Shadows of air in the soft tissues are sometimes found on films of the same types of injury, in cases of surgical emphysema, and after irrigation or cleansing with hydrogen peroxide.

(5) All roentgenograms of injuries in which

the skin is broken should be examined for the presence of shadows of gas.

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DISCUSSION (*Abstract*)

Dr. D. Y. Keith, Louisville, Ky.—In the surgical and clinical diagnoses reported, there was a death rate of approximately 52 per cent; while from the x-ray diagnoses there was a death rate of 22 per cent. So you see the very marked value of an x-ray diagnosis.

All of us who have had very much experience in x-ray work make a report of any free gas shown. We see that often though it is small, and we recommend a re-examination at a very early time. We can thus pick up gas infection and we shall be able to say within a few hours' time definitely whether air or gas are present in the soft tissues. Often we can estimate the virulence of the infection, particularly if we are allowed to examine the patient in a few hours' time, and can tell the amount of gas present. If we can say only, "This is a very virulent type of infection," it helps with the diagnosis and prognosis.

I believe I can tell from films the difference between air infection and gas-bacillus infection with some degree of accuracy. You get a different distribution of the radiolucent shadow where air and where gas are present.

Dr. J. W. Pierson, Baltimore, Md.—I did not know that big men were so susceptible to infection.

Dr. F. K. Herpel, West Palm Beach, Fla.—Particularly in traumatic surgery, it seems to me vitally important that the x-ray show all the soft tissues.

I saw an x-ray picture of a young colored man who was shot with an old pistol. The picture was taken about two hours and a quarter after the injury. He already showed small globules of air over the leg and infiltrating up along his leg. He died the following day with an acute gas infection.

In another instance, a youngster, the morning following a simple fracture of the humerus with a minute abrasion, showed definite gas over the humerus. He died the same afternoon.

Dr. J. T. McKinney, Roanoke, Va.—The roentgenologist should ever be on the alert to see and report air when it is found on the film. I recall the case of a patient who came in from Asheville, North Carolina, with apparently an acute abdominal condition. She was x-rayed, and a few bubbles of air were seen in the soft tissues on the left side, just above the ileum. We were able to determine that the air was due to a perforation of a retroperitoneal diverticulum of the sigmoid, the few bubbles of air giving us the clue in making a diagnosis.

Dr. Keith.—Has Dr. Rhinehart made any films of these patients just before they died? One of our patients with a gas-bacillus infection died on the fourteenth day after his injury with air in the cranial cavity. His eyes protruded out of the orbital cavity and I am sure the sutures were separated.

Dr. Rhinehart (closing).—We have, of course, seen patients with free gas in the peritoneal cavity from ruptured viscera, and in one interesting instance following a self-induced abortion. In gas-bacillus infection it is of the greatest importance that the patients be examined soon after the injury. In my paper I tried to emphasize the diagnostic importance of x-ray examinations in gas-bacillus infections, the control of the treatment by x-ray observations, and the prognostic benefit of such early recognition and treatment.

A PRELIMINARY REPORT OF TWENTY-THREE CASES OF CORNEAL OPACITIES TREATED WITH SURGERY AND RADIUM*

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and
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Preservation of sight, not only in the new born but also in individuals of all ages, has been the aim of physicians from time immemorial. Gibson of England, during the early part of the Nineteenth Century, pointed out that proper treatment of expectant mothers and prompt removal of soilage from the eyes of the new born and irrigation of these eyes would prevent infection. Crede some 89 years later reduced the morbidity from 10 to 0.5 per cent by the well known prophylactic treatment.

Royer[1] recently stated that statistics based

*Read in Section on Ophthalmology and Otolaryngology, Southern Medical Association, Twenty-Fourth Annual Meeting, Louisville, Kentucky, November 11-14, 1930.

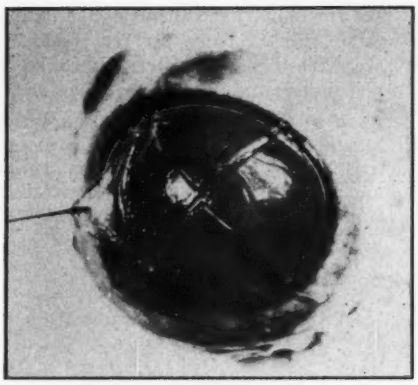

Fig. 1
Ox eye showing crucial incision in cornea made with scalpel with one segment resected. (After Wiener.)

on admission to schools for training the blind, in 1908, showed that 28 per cent of the patients had lost their vision from birth infections. In 1929, the number of these cases had been reduced to 9 per cent. The figures in the Texas State School for the Blind are somewhat higher, being from 16 to 18 per cent. It is interesting to note that Mark Stevenson showed some years ago that only 60 per cent of birth infections were due to the gonococcus, while the other 40 per cent were due to various bacteria such as streptococci, staphylococci, or pneumococci.

The purpose of this paper is to give a short preliminary report of some of the work that has been going on at the Texas State School for the Blind during the last two and a half years.

In 1926-27 Meyer Wiener described an operation that he had performed on a number of corneal opacities, which was followed by remarkable improvement in sight. As we have followed Weiner's technic almost exactly, we will quote his description of the operation:

"Under cocaine anesthesia a crucial incision was made through the scar with a small sharp scalpel, the incision extending almost to the margin of the cornea, both vertically and horizontally. The incision was made as deep in the cornea as possible without penetrating through into the anterior chamber. The apex of one of the quadrants was then lifted up with a small sharp iris hook (so-called dural hook), and with the sharp scalpel, carefully dissected back toward the base of the triangle, great care being taken to keep in the same corneal layer as that in which we started. This is very readily done, as the line of cleavage between the corneal layers can easily be seen when making traction on the segment. The dissection is started by making traction with the hook until enough has been loosened to enable one to grasp firmly with a fixation forceps. As soon as the segment is dissected to the base of the triangle, it is cut off from its attachment. In a similar manner each of the remaining three segments is resected, thus freeing the cornea of its scar tissue. The after-treatment is simple. Atropine was instilled, a small quantity of xeroform powder dusted over the denuded area and a dry gauze dressing applied."

In the fall of 1927, Weiner's operation was performed on some of the children at the Texas School for the Blind with encouraging results.

Following this operation, the patients suffer practically no pain and the wound is healed in from 7 to 10 days. The results in these early operations were sufficiently gratifying to justify the continuance of this work, for in each and every case there was an improvement from increased light perception to the ability to observe objects.

In connection with the regeneration of the cornea, Rucker has recently reported the results of his work in which he excised part of the cornea, noting that the epithelium had grown over the denuded surface at the end of a week. However, he also observed that the cornea usually broke down within a few days, sometimes at the center and sometimes near the periphery. These ulcers were about 1 mm. in diameter and healed rapidly except when they became infected.

Rucker's observations regarding the regeneration of the cornea over the raw surface substantiate our observation, for while in his work the corneae of normal rabbits were used, our subjects were patients with old corneal opaci-

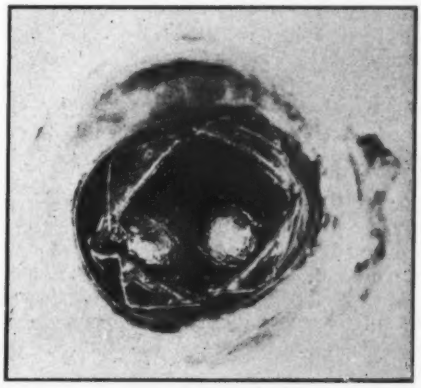

Fig. 2
Ox eye with the four segments dissected away. (After Wiener.)

Fig. 3
Shows thick irregular corneal epithelium and scar tissue. This case had never been treated before.

ties, and the wound becomes covered with corneal epithelium instead of scar tissue. We have also observed under the slit lamp that the density of the scar tissue is thinner following the operation and that this is due to the fact that the corneal epithelium regenerated more rapidly than does the scar tissue (connective tissue).

Meyer Weiner found in his cases that the resected cornea became thinner with time and took on more of the characteristics of normal corneal epithelium. (That this occurs has been forcibly impressed on us by the results in our cases.)

In spite of the gratifying improvements following these operations, there was still much to be desired, and since Lane and others had reported favorably on the results obtained with radium in cases of corneal opacities, in May, 1929, we started using radium on these cases. The technic used was the same as described by Dr. Laura Lane. During the early part of this procedure, the patients received weekly treatments of 10 mg. of radium element for two and one-half, three and three and one-half minutes, respectively, passed to and fro from 1-2 mm. above the cornea. Following the third application, the radium treatments were given every three weeks. The dosage has since been changed to three, four and five minutes for the first three treatments, and then for five minutes every three weeks. Three per cent cocaine is used as an anesthetic and silver plated lid retractors to protect the lids and give exposure.

In regard to the action of radium on various tissues, Sanford Withers notes five structural characteristics which determine the susceptibility to radiation, all of which are of a cellular nature:

(1) Undifferentiated form of cells
(2) Rapid growth with abundance of mitoses
(3) Large hyperchromatic nuclei
(4) Vascularity, especially when due to an abundance of thin-walled capillaries.
(5) Absence of stroma or intercellular substances.

He also states that scar tissue appears to be more sensitive than normal tissue, and it is possible to cause a marked softening in old scar contractures by erythema doses of radiation. These observations confirm our reasoning, in that we are dealing with thin-walled vascular scar tissue, which reacts favorably to radium.

There are two points that are of the utmost importance in treatment of these cases of corneal opacities: (1) by literally shaving off as much scar tissue as possible, the opacity is thinned because the corneal epithelium regenerates more rapidly than does the scar tissue; and (2) the gross removal of the tissues prevents the cells from becoming radio-inactive due to repeated radium treatments.

Fig. 4
Corneal epithelium thinning out.

The following 23 cases are composed of 15 pupils from the Texas State School for the Blind and 8 private patients. The histories, examination findings and treatment are condensed for the sake of brevity.

Case 1.—A. J. B., age 9, had the history of sore eyes in infancy. Examination shows marked lateral nystagmus, bilateral staphylomatous corneae with large opacities. Iridectomy has been done at 12 o'clock in each eye. With the right eye he counts fingers at 1 foot. With the left eye he counts fingers at 8 inches. Corneal opacities were diagnosed, with bilateral staphyloma due to ophthalmia neonatorum.

Fig. 5
Corneal epithelium becoming more stratified.

(Because of the exact similarity between the two eyes, only the left eye has received the routine treatment. The right eye has been kept as a control. At the present time, the left cornea has flattened and rounded out, resuming a normal shape, and the staphyloma has disappeared, and the entire appearance of the globe has returned to normal as far as the staphyloma is concerned.)

This patient has had three scaling operations on the left eye, 13 radium treatments, and a total of 56 minutes' exposure to 10 mg. of radium element in a platinum needle. The vision in the left eye is 2/200.

Case 11.—N. S. S., age 19, had a history of sore eyes in infancy. Examination showed a very irregularly shaped cornea and corneal opacity on the left eye. The left eye had light perception. The right eye had been enucleated.

This patient has had three scaling operations and 22 radium treatments totalling 105.5 min. She now counts fingers at 14 inches. This is one of the most remarkable cases that we have had, because there was practically nothing to start with. The corneal opacity has now become more round than oval, the dark iris can be seen in the background, and the opacity has thinned greatly.

Case 12.—W. A., age 35, had a history of sore eyes in infancy. Examination showed a phthisis bulbi in the right eye with marked corneal opacity. The nystagmus

Fig. 6
Corneal epithelium more stratified.

Fig. 7
Same as Fig. 6

Name	Vision Before Treatment	No. Operations	No. Radium Treatments	Amt. Rec'd	Vision 9-30-30
1. AJB	LEV fingers 8 in.	Two	13	56 min.	2/100
2. NOM	LEV hand motion 1 ft.	One	16	69½ min.	Hand motion 4 feet
3. EMS	LEV light perception	One	16	69½ min.	Hand motion 4 feet
4. TS	LEV light perception	Two	12	51 min.	Hand motion 12 in.
5. NS	LEV light perception	Two	16	71 min.	Hand motion 20 in.
6. HB	REV hand motion 12 in.	Two	15	66 min.	2/200
7. LP	LEV hand motion 6 in.	One	11	52 min.	Hand motion 5 feet
8. ZT	LEV hand motion 12 in.	Two	13	57 min.	Hand motion 12 in.
9. EP	LEV hand motion 6 in.	One	16	69½ min.	Hand motion 30 in. Did not return
10. ZMG	REV light perception	One	7	26 min.	Dropped because of normal LE
11. NSS	LEV light perception	Three	22	105½ min.	Counts fingers 14 in.
12. WA	REV hand motion 6 in. LEV 2/200	Four One	18 24	86 min. 98 min.	Hand motion 10 feet 5/200
13. JOG	REV light perception	One	4	16 min.	Hand motion 2 in. 11-5-20 stopped
14. MLB	LEV light perception	One	4	17 min.	Improved light perception
15. RH	REV light perception	One	6	27 min.	Light perception improved
16. LAH	Counts fingers 3 in.	One	2	8 min.	1/200
17. HCB	20/200	One	1	3 min.	20/200
18. LMG	REV light perception	One	9	42 min.	Dropped. Did not return
19. TB	REV light perception	One	3	8½ min.	Light perception improved
20. EP	REV light perception	Four	9	42 min.	Hand motion 21 in.
21. MLL	REV light perception	One	6	28 min.	Hand motion 24 in.
22. MLG	REV light perception	Two	7	33 min.	Hand motion 8 in. Dropped
23. WWN	LEV light perception	Two	10	41 min.	Hand motion 6 in.

was also great. In the right eye there was light perception. The left eye was normal in shape, but there was a large corneal opacity, which covered two-thirds of the surface. An iridectomy had been done at 6 o'clock, which gave the patient 2/200 vision.

In the right eye, there had been four operations, 18 radium treatments, totalling 86 min. The right vision is now hand motion at 10 feet. The left eye has had one operation, 24 radium treatments totalling 98 minutes and the left vision is 5/200.

In conclusion, we can do no better than to quote Meyer Wiener's closing paragraphs:

"I believe there are a great number of helpless blind who could be given useful vision if the method of corneal resection were in more general use. The technic is difficult, but can easily be acquired by practice on dead animal eyes, as I have often demonstrated to post-graduate students. Even if one is not helped so that he can read, it is a tremendous advantage to be able to see a little.

"The advantage of resection over trephine transplantation lies in the fact that the technic is simpler and there is practically no danger of sepsis. Where antiseptics are used as in resection, a graft is apt to be destroyed by them. Failure to obtain a clear spot means that one can repeat the performance later and attempt to get into a layer deep enough to reach beyond the opacity. Should perforation occur, one halts and proceeds again later, after the opening has healed."

Figures 1 and *2* are taken from Meyer Wiener's article showing the crucial incision in the cornea and the four segments dissected away.

Figure 3 shows the thick, irregular, uneven corneal epithelium and the very vascular scar tissue between. This case had not been treated previous to this operation.

Figure 4 shows that the corneal epithelium is flattening out in the center, but that there is still quite a great deal of thickness and irregularity in the cells.

Figures 5, 6 and *7* show how the cornea has regenerated and approached normal following repeated operations and radium treatments.

We wish to take this opportunity of expressing our gratitude to Drs. Laura Lane, Hiram Woods, S. W. Bohls, D. C. Peterson and J. Warren Jackson for their valuable suggestions, criticisms, and assistance in this work.

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DISCUSSION (*Abstract*)

Dr. Charles D. Townes, Louisville, Ky.—Too often we may be prone to look upon these poor unfortunates as being past any aid and give them a prognosis of having to spend the rest of their days in almost total blindness, or with a degree of vision insufficient for them to perform any useful work. These patients, who have much to gain and little to lose, should be given the benefit of every procedure which may restore to them some degree of vision. Even an improvement from light perception to the ability to discern objects, slight as it may seem to us, is one for which they will be forever grateful.

In my opinion the surgical procedure described by Dr. Hilgartner, namely, "scaling" or dissecting off as much of the opaque cornea as possible, is the method of choice. The epithelium regenerates rapidly and the thinned cornea actually becomes less opaque as time passes.

Transplantation of clear corneal substance has not been so satisfactory as was hoped for because in time the transplant becomes as opaque, practically, as the corneal substance which was removed to make place

for it. Besides, as Dr. Hilgartner brought out, there is more likelihood of infection.

In the application of radium to follow up the operation it is of interest to note that small doses of radium have been used. This point is of the utmost importance. A great many cases of untoward, even disastrous results, have followed the use of larger doses of radium, either, as in earlier days, improper use of radium, or in some cases influenced by the particular individual reaction of the patient, in some manner little understood.

There is undoubtedly great benefit to be derived from the use of radium in ophthalmic conditions, especially in the treatment of such cases as Dr. Hilgartner has reported this morning, but extreme care should be observed in the selection of dose and of screening. More cases must be treated in this manner and results reported carefully before we can have a true idea of the value of the procedures.

Dr. Meyer Wiener, St. Louis, Mo.—Vascularity is one of our chief obstacles in the surgery of corneal scars, and here radium may be a factor in improvement of results. While radium may not prove of much value in old scars, it has a definite place in recent scars. Allen Robinson states that keloids of the lids respond to radium therapy. The earlier the treatment is applied to the hypertrophic scars the quicker are results obtained, as the young fibroblasts with a collagen matrix are radiosensitive. Dense firm scars are radioresistant. He suggests excision followed by radium to prevent recurrence. There is a definite indication for radium in conjunction with plastic operations on the lids and face. The beginning of Hilgartner's work antedated Robinson's suggestion by nearly two years.

While the authors' results are not startling, they do show a definite improvement in a few cases, all of which were desperate, with no hope of gain by any other method. As they had nothing to lose, any gain may be counted an advantage. I have not noticed the tendency observed by the authors for the epithelium to break down in the center. There have been a few cases where the central portion of the resected area has been slow to epithelialize. This has always been corrected by instillation of 1 per cent aniline red, which stimulated the epithelium to grow.

Minowada has reported on the stimulating effect of thyroid extract on regeneration of corneal epithelium (*Act a dermat.*, 11:437, May, 1928).

While I believe that the Drs. Hilgartner have given us a thought which promises a better prognosis in corneal scar surgery, it must be borne in mind that the use of radium is not without its danger. Warty conditions of the conjunctiva, invading the cornea, have been reported following repeated exposure to x-ray or radium (E. T. Collins, *Tr. Oph. Soc. U. Kingdom*, 48: 8285, 1928).

I have seen cold ulcer of the cornea resulting from radium exposure in the treatment of vernal catarrh. The authors are to be congratulated for their boldness in attacking this most difficult problem and for opening a way to hope for valuable improvement over known methods.

Dr. Hilgartner misunderstood one passage in my article. He said that I noted a thinning in the cornea. There is a thinning of the epithelium, but not the cornea. There is a thickening of the cornea and a definite beginning regeneration and thickening of the corneal tissue.

Dr. Phil M. Lewis, Memphis, Tenn.—I should like to know if there is any danger in doing this operation, of starting sympathetic ophthalmia or uveitis or anything of that sort. I should also like to know, in cases such as Dr. Wiener had, with 15/40 vision, what sort of refractive error these cases had, if an astigmatic correction with ordinary cylinders can be worked out in those cases if the cornea has a relatively smooth contour. I should also like to ask if these eyes are more prone to ulceration and infection than the ordinary eye.

Dr. Hilgartner (closing).—I have seen no evidence of danger of sympathetic ophthalmia.

As to refraction, of course these cases are hopeless. Most of them have resulted from ophthalmia neonatorum. The iris and cornea are adherent, so that refraction has not come into the question at all, as the cornea is not cleared up enough for glasses. I have thought these cases were more prone to ulceration than others.

Dr. Pfahler, of Philadelphia, last year at Detroit, suggested that I use a radium needle, put it in direct contact with the cornea, leave it there only about fifteen seconds at first, and then possibly increase the time gradually. I have been a little afraid to do that, but it is our intention to try it on cases where we can do no harm.

KRUKENBERG TUMORS AND OTHER SECONDARY OVARIAN CARCINOMAS*

By J. MASON HUNDLEY, JR., M.D.,
Baltimore, Md.

In attempting to review the subject of Krukenberg tumors it soon became evident to me that this was impossible without a study of all secondary ovarian carcinomata. Prior to 1900 these secondary ovarian growths were considered very unusual, Rokitansky being one of the first to report such tumors metastasising from primary lesions in the stomach, breast and uterus.

In 1896, Friederich Krukenberg published his paper on "Fibro Sarcoma Ovarii Mucocellulare (Carcinomatodes)." The characteristics that he noted are as follows: the tumors are solid though areas of cystic degeneration are often seen. They grow slowly, retaining the shape of the ovary and the surface may be smooth or lobulated like a fetal ovary. They may be single, but are usually bilateral and may grow to a large size. In his first case reported, the right ovary measured 12 x 8 cm. and the left measured 10 x 6 cm. They may occur either in youth or old age and ascites

*Read in Section on Gynecology, Southern Medical Association, Twenty-Fourth Annual Meeting, Louisville, Kentucky, November 11-14, 1930.

*From the Department of Gynecological Pathology of the Johns Hopkins Hospital.

Fig. 1

Carcinomatous nodule in substance of ovary, primary focus being in the breast. An example of lymphatic dissemination. Gen. Path., J. H. H., 5406. X 120

is usually present. On microscopic examination there is seen a well marked connective tissue framework with interlacing fibrilli and areas of myxomatous appearance. He says: "The chief characteristic of the tumor was the inclusion of large, roundish cells blown up like bubbles in the fine tissues between the fibrilli of the connective tissues, best seen in the myxomatous-looking areas. The nucleus was out of center, giving each cell the appearance of a sealing ring. The largest had a diameter of about 0.016 to 0.022 mm. The markedly swelled body was homogenous, clear and transparent. Besides these there were smaller round cells and transitional forms free in the connective tissue. The large cells probably grew out of the smaller by mucous metamorphosis."

Krukenberg was not completely satisfied with his interpretation of the origin of this tumor which is indicated by the attribute carcinomatodes. He at first considered that the growth was epithelial in origin, for the lymph channels were found filled with cells which closely resembled epithelium. He also tried unsuccessfully to trace their origin from the Graffian follicles and their embryonic remains. However, we see that in his final analysis he believed that they had their origin in the connective tissue. The true nature of these tumors was not made clear until Schlagenhaufer brought out his work in 1902 on metastatic ovarian carcinoma following cancer of the stomach, intestine and other abdominal organs. He collected from the literature 71 cases of secondary carcinoma of the ovary and added 8 of his own. He found 61 with cancer of the stomach, 10 with cancer of the intestine, 7 with cancer of the gall-bladder and 1 with cancer of the adrenal.

From the study of his 8 cases he concluded that the Krukenberg tumor was epithelial in origin and was of a secondary type arising most frequently from cancer of the stomach. In 5 of his cases there was definite histological evidence of the direct connection between the primary growth in the stomach and the secondary in the ovary. He also showed that the corresponding lesions in the same patient were identical in histologic structure, although the ovarian growths varied one from another. In this series there were only 2 typical Krukenberg tumors found.

Glockner was also in accord with the views of Schlagenhaufer. He reported 17 cases of secondary ovarian cancer, the primary tumors occurring as follows: 7 in the stomach, 5 in the breast, 3 in the uterus and 2 in the lower portion of the large bowel. Bland-Sutton believes that metastatic ovarian cancer, in one or both ovaries, is fairly common, occurring in 10 per cent of autopsies for gastric or mammary cancer. He is also of the opinion that primary cancer of paired organs is almost invariably unilateral. However, Ewing states that the majority of ovarian carcinoma are originally bilateral or soon become so, and this latter opinion, I believe, is universally upheld.

In reviewing the literature on Krukenberg tumors one often has great difficulty in deciding whether the secondary ovarian growth reported is of the type described by Krukenberg or whether it falls into the other classes of the group, namely, the medullary, the scirrhus or adenocarcinoma. When I began this study I was under the impression that all solid bilateral carcinomas of the ovary secondary to a malignancy of the stomach or intestine were Krukenberg tumors, but I soon found that the conception was erroneous, for the most common secondary tumor from this source is the adenocarcinoma.

ROUTES OF METASTASIS

According to Frankl, metastasis into the ovaries from various organs may occur in different

Fig. 2

Section of ovary showing metastasis on its surface, the primary focus being in the breast. This illustrates dissemination by implantation. Gen. Path. J. H. H., 5850. X 75

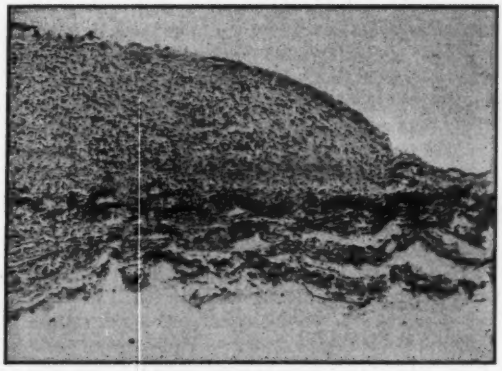

Fig. 3

Carcinomatous nodule seen on peritoneum, this being part of an extensive abdominal carcinosis, the primary focus being in the breast. Gen. Path. J. H. H., 6017. X 75.

ways, depending on the situation of the primary focus. He classifies the primary tumors into three groups according to their location.

1. Those which have no topical relation to the ovaries, such as the mammary gland and the thyroid.

2. Those which have a partial topical relation such as the stomach, intestine, adrenal and gall-bladder.

3. Those that have a close relation to the ovaries, such as the uterus, tubes and rectum.

We will now consider, somewhat in detail, these different subdivisions.

GROUP ONE

In dealing with an abdominal growth of uncertain origin the breasts should be carefully examined, for a small scirrhous carcinoma may be found and, according to Ewing, this type of growth is prone to widespread metastasis.

The manner in which this dissemination takes place is of great interest and has been exhaustively studied by Handley. He has shown in his work on cancer of the breast that the abdominal infection may occur by several pathways, the most common being by epigastric invasion. By this route the growth spreads by lymphatic permeation and the vessels lying on the anterior sheath of the rectus in the right epigastric angle soon become engorged and the cancer cells then pass down to the liver by way of the falciform ligament. The cells then escape into the peritoneal cavity and multiple metastases soon develop. Handley believes that this method of invasion of the abdominal organs is common, occurring 53 times in 422 autopsies, the lungs being free, which indicated that the extension did not pass through the thorax. The next most frequent path of invasion is by the retroperitoneal route. By direct extension of the breast cancer through the chest wall the pleura frequently becomes infected with a resulting ex-

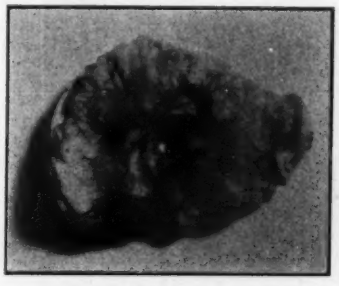

Fig. 4

Section showing perforated ulcer of the stomach. Surg. Path. J. H. H., 40248.

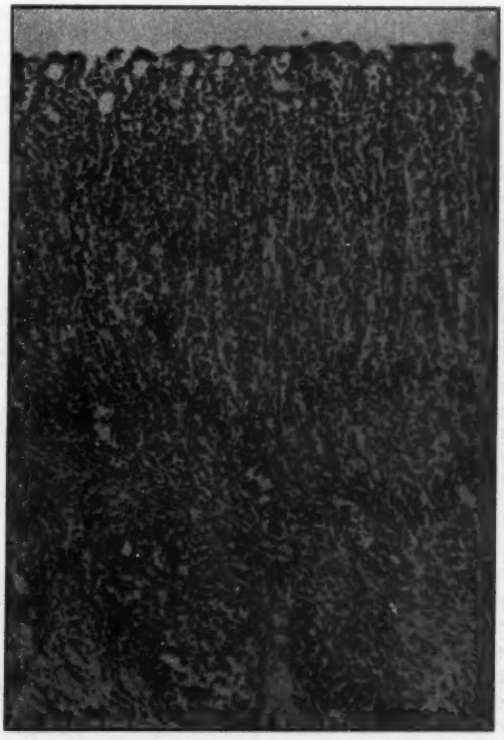

Fig. 5

Section taken from base of perforated ulcer shown in Fig. 4. Medullary carcinoma seen deep in the tissues. Surg. Path. J. H. H., 40284. X 75.

Fig. 6

Section showing a Krukenberg tumor of the ovary. Carcinoma in base of ulcer shown in Fig. 5, being the primary focus. Many large signet cells are seen. Women's Hosp. Gyn. Path. 4922. X 480

tension to the sub-pleural lymphatic plexus. Later the lymphatics of the diaphragmatic crura, which carry lymph to the lumbar glands, become involved and it is by this means that we have invasion of the retroperitoneal structures. With the lumbar lymph nodes involved, it is quite possible to have the ovaries infected by retrograde lymphatic dissemination. In rare and late cases of cancer of the breast the abdomen may be invaded from the thorax by direct infiltration of the diaphragm.

GROUP TWO

In this division the primary growths are located in the abdominal cavity. The stomach and the large intestine are the organs most frequently involved, as is shown in Stone's collection of 133 cases of secondary ovarian cancer. He found 75 with cancer of the stomach, 22 with cancer of the large intestine, 4 with cancer of the small intestine, 5 with cancer of the gall-bladder, and 1 with cancer of the appendix.

The manner in which the malignant cells of the primary growth reach the ovary has been the subject of much discussion and speculation. The two most likely routes are by direct implantation and by the lymphatics.

In the theory of implantation, with the focus in the stomach or intestine, it is thought that the cancer cells perforate the serosa and are then set free in the peritoneal cavity. By gravity and the peristaltic action of the intestines they then settle on the ovaries and into the *cul-de-sac* of Douglas. With the cancer cells free in the abdomen, involvement of the viscera soon takes place, and this is usually associated with the production of ascites.

This theory was first elaborated by Bucher (Stone) and is supported by Schlagenhaufer, Kraus, Amann, Handley, Bland-Sutton, and others. I would here like to quote Bland-Sutton's poetic description of implantation. He says: "In this way the ovaries may be pictured as receiving a light covering of cancer cells, as evergreen shrubs are clothed by snowflakes in winter."

Kraus, in 1901, showed fairly conclusively that India ink injected into the peritoneal cavity of rabbits permeated the surface epithelium

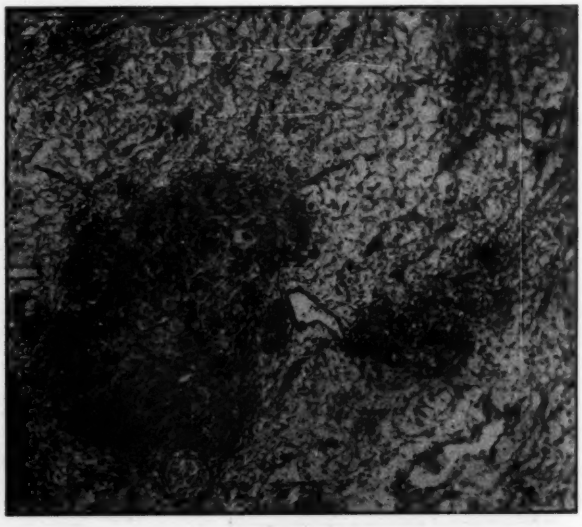

Fig. 7

Krukenberg tumor of the ovary. Low power showing nest of signet cells surrounded by fibrous tissue network. Gyn. Path. J. H. H., 29491. X 75.

of the ovary and Sitzenfrey has also reported finding cancer cells between the germinal epithelium. However, Wolffheim's experiments did not entirely support these views, for he showed that the germinal epithelium was resistant to cellular invasion except where the continuity was broken up by the rupture of a Graafian follicle.

I am of the opinion that implantation of the ovary does occur, but only when there is an associated abdominal carcinosis. Under these conditions the ovary is invariably covered with a nodular growth and a similar condition is often found on the uterus and in the *cul-de-sac* of Douglas.

It is difficult to see how the Krukenberg tumor which gives the appearance of a large ovary with a smooth surface could have been formed by the implantation method of dissemination. It would appear that this type of tumor is formed by lymphatic metastasis from the stomach to the lumbar glands by way of the subpyloric plexus. With the lumbar glands involved it is thought that by retrograde dissemination both ovaries are infected through the hilus and in this way the surface of the ovary remains smooth and free of papillary growths.

GROUP THREE

In this group of our subdivision we include the primary growths that are in close relation to the ovaries, namely, the uterus, tubes and rectum. The commonest uterine growth that metastasizes to the ovary is the adenocarcinoma and this is relatively infrequent, for Schotllander found only 3 instances of ovarian involvement in 140 cases of adenocarcinoma of the uterine body. Norris and Vogt report only 2 ovarian cancers in a series of 115. I find it is occasionally stated that the Krukenberg tumor may be secondary to a carcinoma of the uterine body, but I am unable to find a single instance of such an occurrence.

As stated above, carcinoma of the large bowel as a primary focus for the ovary is not uncommon. When the growth is confined to the rectum the ovarian involvement is by direct extension through the bowel wall. However, when the focus is in the large intestine the dissemination is undoubtedly by the lymphatics. In some cases of intestinal cancer the pre-aortic lymph nodes soon become involved, for these structures receive all the lymph of the alimentary tract. With their involvement, as we have shown, the ovaries may be involved by retrograde dissemination.

REPORT OF CASES

For this study I have been able to collect 27 cases of secondary ovarian cancer occurring in the Department of General Pathology and Gynecological Pathology at the Johns Hopkins Medical School. On reviewing 11,200 consecutive autopsies I was able to find 15 such tumors. The remaining were obtained from the Gynecological Department. Tabulation of the primary growths is as follows: there were 5 with cancer of the breast, 8 with cancer of the stomach, 4 with cancer of the rectum, 2 with cancer of the large bowel, 1 with cancer of the gall-bladder, and 7 with cancer of the uterus.

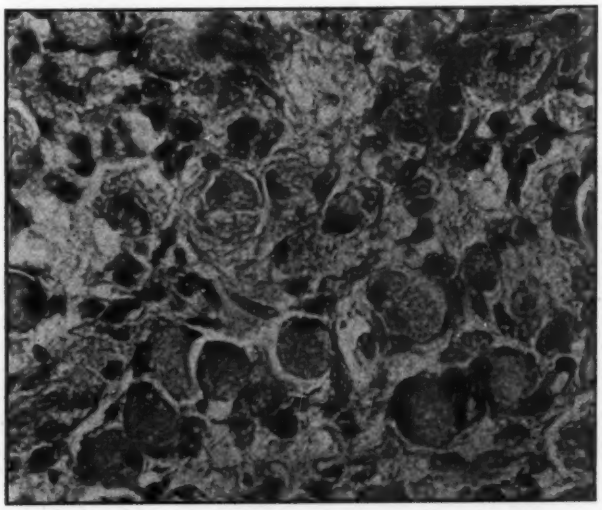

Fig. 8
High power of the same tumor showing many signet cells. Gyn. Path. J. H. H., 29491. X 480.

SUMMARY OF FINDINGS WHEN THE PRIMARY GROWTH IS IN THE BREAST

In 59 autopsies for cancer of the breast there were found 5 instances of metastasis to the ovary. The average age of the patients, 4 of whom were colored, was 36 years. Two of the breast cancers were of the scir-

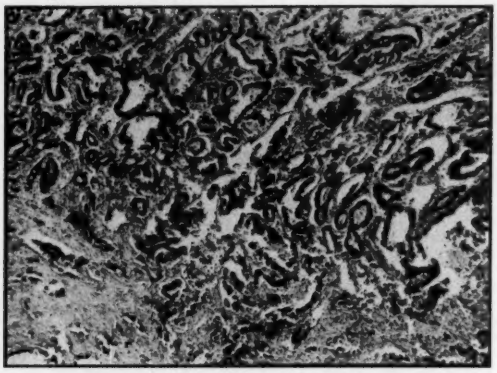

Fig. 9
Adenocarcinoma of lower end of ileum. Gen. Path. J. H. H., 11123. X 75.

rhous variety and were associated with widespread metastases, this being a rather frequent finding with this type of mammary cancer. The three remaining cases were of the medullary type and in all 5 the primary and secondary growths rather closely resembled one another. In considering this group from the viewpoint of Handley's theories of lymphatic permeation we find no instance of ovarian or abdominal metastasis that could be accounted for by epigastric invasion. All of the autopsies showed thoracic infection, the lungs being involved four times. In these cases the invasion of the abdomen was by way of the retroperitoneal route, that is if one is in accord with the views of Handley. When there is such widespread dissemination one cannot help but feel that the blood stream must play a part in its production.

The different ways in which the ovary may be involved was shown in two cases. One ovary showed a carcinomatous deposit on its smooth surface, thus illustrating dissemination by implantation, while the other ovary showed a metastatic nodule deep in the cortex surrounded by normal tissue. This last finding could either be accounted for by lymphatic or blood stream metastasis, the former being most likely.

SUMMARY OF FINDINGS WHEN THE PRIMARY GROWTH IS IN THE GASTROINTESTINAL TRACT AND GALL-BLADDER

In the review of 11,200 autopsies, in order to determine the incidence of visceral carcinoma metastasizing to the ovary, several interesting facts were brought out. There were found 181 autopsies for carcinoma of the stomach, 145 being in the male and only 36 in the female, and of these 36 primary carcinomas there were 3 that had metastasized to the ovary, giving an incidence of 8.3 per cent. The figures on the incidence of metastasis vary greatly. Borrman (Ewing) states that this occurs in 2.3 per cent of cases, whereas Bland-Sutton finds metastasis in 10 per cent of his autopsies. In this completed group there are 8 patients with primary carcinoma of the stomach, 2 in the ileocecal region and 1 in the gall-bladder. Out of this number 3 Krukenberg tumors were found. However, it is due to the interest in this type of growth that so much attention has been focused on all secondary ovarian carcinomas. In the 8 patients with the primary growth in the stomach the ages ranged from 31 to 70. In all of these the outstanding symptoms were: pain in the epigastrium, nausea, vomiting, and loss of weight. The symptoms referrable to the pelvis were not prominent.

Of the four women in the productive period all complained of dysmenorrhea, whereas only one showed any menstrual irregularity, that being menorrhagia and metrorrhagia. This is rather surprising, for ovarian carcinoma is a frequent cause of uterine bleeding before or after the menopause. Of the eleven patients in this group, all died and eight came to autopsy, the diagnosis in the remaining three cases being made at operation. On microscopic examination of the neoplasms there were found five adenocarcinomas, two medullary carcinomas, one scirrhous carcinoma and three typical Krukenberg tumors. The primary and secondary tumors resembled each other fairly well. As Kru-

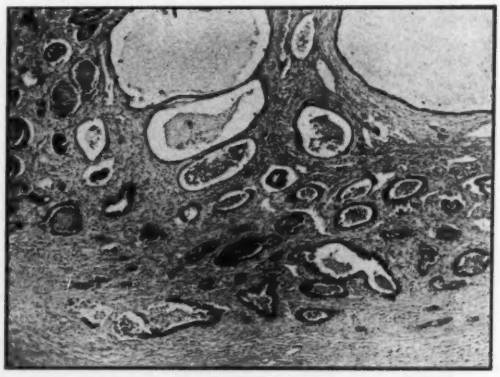

Fig. 10
Section of ovary showing metastatic adenocarcinoma, the primary focus being in the intestine as is shown in Fig. 9. Gen. Path. J. H. H., 11123. X 75.

kenberg tumors are uncommon, I would like to submit the findings in my three cases. I am greatly indebted to Dr. J. J. Seegar and Dr. J. G. Murray, of Baltimore, for permission to make this report.

Mrs. E. R. C., age 31, at 3 a.m. on March 3, 1928, underwent an emergency operation by Dr. Seegar. Three hours previously she had been seized with a severe pain in the abdomen. The pain was diffuse in character and came on after eating. On opening the abdomen and exposing the posterior wall of the stomach a perforated ulcer surrounded by an indurated mass was found. The ulcer and area of induration was excised and the patient made an uneventful recovery. At that time there was no evidence of metastasis. The microscopic report from Dr. Joseph Bloodgood's laboratory was as follows: the tissues below the base of the ulcer were everywhere infiltrated with cancer cells, some growing in columns and others showing glandular arrangement. The cells are actively invasive, many mitotic figures being seen. The diagnosis was medullary carcinoma.

Three months following the first operation the patient began to complain of increasing tenderness and enlargement of her abdomen associated with nausea. She was seen by Dr. Murray and he was of the opinion that she was probably pregnant, although no menstrual period had been missed. In a few weeks the abdomen became markedly distended with fluid and the physician was able to map out two large pelvic masses on either side of the enlarged uterus. Dr. Seegar again operated, and on opening the abdomen about three liters of straw-colored fluid escaped. The ovaries were changed into large tumor masses which had smooth surfaces and still retained the shape of the ovary. A bilateral salpingo-oophorectomy was done and the patient did well for a short time, but unfortunately developed an intestinal obstruction and died. A partial autopsy showed an indurated mass in the stomach with many metastatic nodules in the upper abdomen and in the omentum.

The microscopic examination of the pelvic tumors showed a medullary type of growth which occupied the whole central portion of the ovary. The fibrous tissue framework was quite meager and there were no areas of myxomatous appearance. However, throughout the section many beautiful signet cells were seen with pink staining cytoplasm and extra-centric nuclei. The malignancy in the stomach and ovary closely resembled one another with the exception that no signet cells were seen in the primary growth.

The data on the second case of Krukenberg tumor which follows is quite meager, but sufficient, I believe, to make a correct diagnosis.

Mrs. C., age 60, was operated upon by the late Dr. T. B. Johnson, of Frederick, Maryland, for solid ovarian tumors. The tumor proved to be a carcinoma of the Krukenberg type and resembled very closely the description in the above case. At the time of operation there was no mention of a primary lesion in the alimentary tract. However, the record shows that a few months later a gastrointestinal x-ray demonstrated a malignancy of the stomach. The patient died a short time later, no autopsy being obtained.

The medullary carcinomas in this group are similar in every way to those Krukenberg tumors except that they have no typical signet cells, which are pathognomonic of this type of cancer. In one case of medullary carcinoma many large colloid cells are seen, but the nuclei are much larger and are centrally placed. One has the feeling that if there were more colloid in the cell the nucleus would be flattened out and pushed to the periphery, thus forming a typical signet cell.

For the third case we are indebted to Dr. Karl Martzloff, a former resident of the Gynecological Department of Johns Hopkins Hospital. While visiting the Royal Infirmary, University of Glasgow, Scotland, the surgeon, Mr. Hendley, presented him with a specimen of ovary which later proved to be a typical Krukenberg tumor.

The patient was operated upon for large, solid, bilateral ovarian tumors and at operation there was found an unsuspected carcinoma of the stomach. There was marked ascites, but no peritoneal metastases were found. The microscopic appearance of this tumor differed markedly from the two just described. The section showed a fibrous tissue growth composed of interlacing fibrilli, some areas loosely arranged, others more compact. The surface of the ovary is smooth and from

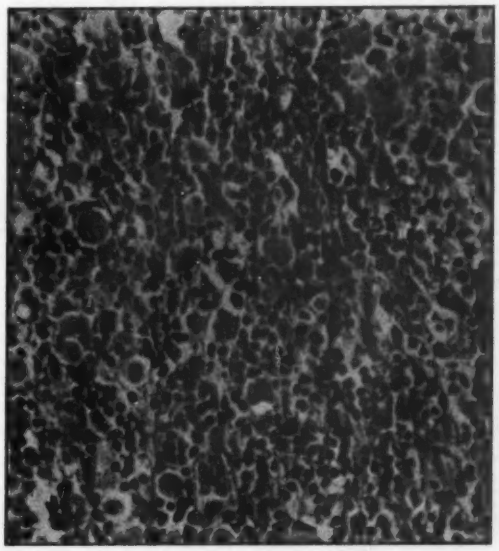

Fig. 11

Bilateral medullary carcinoma of the ovary. Primary focus in the stomach. Many large colloid cells are seen, but there are no typical signet cells found. Gen. Path. J. H. H., 29894. X 285.

it fibrous tissue septa can be seen running toward the hilus. Throughout the growth nests of epithelial cells are seen and scattered everywhere are large pink staining signet cells.

Typical Krukenberg tumors of the ovary are not common, Schlagenhaufer, Glockner and Roemer reporting only 4 such growths in 28 secondary ovarian cancers. According to Stuebler and Brandess (Taylor), 7 Krukenberg tumors were found in their study of 27 ovarian carcinomas, having their origin in the stomach or gall-bladder.

Wagner, in his article on the histogenesis of Krukenberg tumors, is of the opinion that most of the cases are secondary to scirrhous carcinomas of the stomach. This may be true, for my third case showed a definite fibrous tumor and, as the primary and secondary growths are usually similar, we may infer that the primary one was scirrhous. However, the primary and secondary cancers in the first case were proven by autopsy to be medullary and the second case is undoubtedly of the same type.

SUMMARY OF FINDINGS WHEN THE PRIMARY GROWTH IS IN THE UTERUS AND RECTUM

In 1927, Novak reported from the laboratory of Gynecological Pathology at the Johns Hopkins Medical School a study of 174 cases of adenocarcinoma of the uterine body and found metastasis to the ovary in 7 cases. The secondary growths were similar to the parent tumors and were entirely unlike those that originated in the intestinal tract. Since Sampson's work on transtubal implantation there has been some discussion whether the infection of the ovary occurs in this manner or by way of the lymphatics. Novak is of the opinion that the lymphatics are the important route for dissemination.

In regard to carcinoma of the rectum I have collected 4 cases that have involved the ovary, the pathway of invasion being by direct extension. The 4 patients came to autopsy and the microscopical examination of the primary and secondary growths in each case showed adenocarcinoma. Krukenberg tumors having their primary focus in the rectum are uncommon. However, Frankl has reported 3 such ovarian growths, one originating in the rectum and 2 in the lower sigmoid.

CONCLUSIONS

In reviewing the literature on Krukenberg tumors we find that 102 cases have been reported up to this time by the following men: Major, 55; Fallas, 23; Frankl, 12; Stuebler and Brandess, 7; Sacerdote, 1; Hummer, 1; and my report of 3 cases.

It is a well known fact that an organ in which primary cancer arises is rarely the seat of a metastatic cancer and vice versa. However, the ovary is an exception to this, for primary and secondary growths may frequently occur here. Secondary ovarian carcinomas arise most frequently from primary growths in the gastrointestinal tract and the two tumors usually resemble one another closely. The symptoms associated with ovarian cancer arising in the stomach are those of ulcer or malignancy, whereas the symptoms referrable to the pelvis are unimportant. Metastasis to the ovary may occur by way of the lymphatics, by implantation, by direct extension and by the blood stream, the first two routes being the most common. We have shown that all bilateral cancers of the ovary originating in the gastrointestinal tract are not Krukenberg tumors, the majority being adenocarcinomas or medullary carcinomas. The signet cell is pathognomonic of the Krukenberg tumor and may be found in either a medullary or scirrhous type of cancer. On the finding of bilateral solid ovarian tumors one should carefully examine the breasts and

GYN. PATH. J. H. H.	GENERAL PATH. J. H. H.	GYN. PATH. WOMEN'S HOSPITAL
Carc. stomach to ovary	Carc. stomach to ovary	Carc. stomach to ovary
29894	1689	28274
27957	6017	
29491	5607	
21909	Carc. breast to ovary	
Carc. uterus to ovary	7860	
3702	5850	
5768	6695	
8168	5406	
13194	9455	
16115	Carc. intestine to ovary	
18616	11123	
31707	31373 gyn. path. no.	
30530	Carc. gall-bladder to ovary	
34396	11093	
	Carc. rectum to ovary	
	453	
	2116	
	5740	
	3514	

the gastrointestinal tract to rule out a primary focus.

I wish to express my thanks to Dr. T. S. Cullen and Dr. W. G. MacCallum for the privilege of working in their departments.

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DISCUSSION (*Abstract*)

Dr. Bayard Carter, University, Va.—In the review of Krukenberg tumors we necessarily have to take in the adenocarcinomatous tumors. In my experience I have yet to see a true Krukenberg tumor. The diagnosis rests on the pathological section.

One thing which strikes me is the infrequency with which we see adenocarcinoma of the ovary. This may be due to the present day tendency to investigate by curettage all uterine bleeding. I have not seen a true adenocarcinoma of the ovary in three years.

Dr. Hundley spoke of lymphatic implantation, and I think the theory of lymphatic implantation is the one generally accepted. This leads to the clinical point of view that in the present day we must make routine examination of all patients who present abdominal disease. A routine examination of the gastrointestinal tract should be made in all cases. We do this in our service in every instance.

Dr. George Van Amber Brown, Detroit, Mich.—I shall report briefly a case of fibrosarcoma mucocellulare carcinomatodes (Krukenberg type of tumor) operated upon by me about ten years ago. The patient, a woman 57 years of age, the mother of five children living and well, had three miscarriages and had passed her menopause nine years previously. The woman had noticed an enlargement of the abdomen for about one year. There was a history of some loss of weight, strength and appetite. She had no discomfort until about a week before she came to operation. Her chief complaint was a heavy feeling in the abdomen with pain after exertion.

In this case the usual mistake was made of diagnosing an ovarian cyst when dealing with a solid ovarian tumor.

As in Dr. Hundley's cases, upon opening the abdomen a large amount of free fluid was found in the peritoneal cavity. There were two degenerating tumors, regarded at the time as fibroids, each about the size of a grapefruit, presented. One involved the whole of the right ovary, the other the left. The latter mass was readily lifted out without freeing the attachments. The former was more intimately associated and had a broader pedicle. I examined the stomach and breasts carefully, and found no evidence of malignancy. The tumors upon removal were like lead in my hand, very heavy in comparison to other tumors.

One section of the ovary exhibited a peculiar multiplicity of Graafian follicles. The follicles showed both hyperplasia and hyaline change of epithelium. The epithelium in many places showed separation from the stroma. The stroma was a loose reticulum in which were many new shepherd crook form of cells. The second section exhibited the multiple follicles in an older stroma. Through part of the section the connective tissue showed perversion changes with cell division. In a third section there was clearly defined new growth with a rather sharp line of demarcation in which there were outlines of the follicles, all of which were filled with perverted epithelial cells.

My impression is that when solid tumors of the ovary are unilateral the disease is primary in the ovary. If the condition is metastatic, the ovaries are always involved bilaterally.

Another case presented a somewhat different pathological condition.

A woman apparently about forty-eight or forty-nine years of age consulted me three and a half years ago. She had brown spots on her face and quite a marked beard that she had grown in ninety days. She was very loggy, sluggish, slow thinking, slow acting. She also had the male type of distribution of hair over the breasts, abdomen and pubic region. I made a diagnosis of sarcoma of the ovary. The next day we operated and removed a mass as large as a human adult head. The other ovary we left alone. The patient made a nice recovery and, about six weeks later, when she came into the office she had improved mentally, she was not so fleshy and had menstruated, which she had not done for six months. Two months later she appeared in the office again and by that time the hair had left her face, the distribution of hair on the abdomen had become normal, presenting a horizontal line. She was again young and vivacious, apparently her real age, which was twenty-one years.

The pathologist's report in this case was sarcoma of the ovary.

ETIOLOGICAL STUDIES OF GRANULOMA INGUINALE*

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and
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Since 1905, when Donovan[1] described the encapsulated microorganism now generally recognized as being constantly present in the lesions of granuloma inguinale, there has been wide diversity of opinion as to the part played by this organism in the causation of the disease.

Some investigators are of the opinion that the Donovan organisms are not in themselves responsible for the disease, but that they occur in the lesions in association with some other organism, the two probably acting in symbiosis. Others believe the Donovan organism to be the true etiological agent; and during the last few years numerous claims have been made that this organism has been successfully cultivated. In 1911, Flu[2] isolated a gram-negative, nonmotile, encapsulated bacillus from a case of granuloma inguinale. Aragao and Vianna,[3] in 1913, obtained from several cases pure cultures of an organism which they regarded as having the same morphological characteristics as the organisms found in the lesions. They gave to this organism the name *Kalymmatobacterium granulomatis*. E. L. Walker,[4] in 1916, while working in Brazil, cultured from a case of granuloma inguinale an encapsulated bacillus which he classified as belonging to the *Bacillus mucosus capsulatus* group of Friedlander. Walker's work has been corroborated by Randall, Small and Belk,[5] of Philadelphia, who were able to cultivate a similar organism in three of twelve cases studied. Others who have reported the isolation of gram-negative, encapsulated organisms similar to Donovan organisms, and capable of growth on ordinary media are: Lynch,[6] Campbell,[7] Sargent,[8] McIntosh,[9] Goldzieher and Peck,[10] and Castellani and Mendelson.[11] In practically every instance these investigators used Sabouraud's medium in isolating the organisms. None, however, was successful in attempts to induce experimental lesions of the disease by injections of their cultures into animals. Johns and Gage[12] made an extensive cultural study of the disease and were unable to substantiate any claim that Donovan organisms had been cultivated. Later, Gage,[13] working independently, and using Sabouraud's medium, isolated from a case an encapsulated organism with the morphological characteristics of the Donovan organism. He stated that this organism was not identical with the *Bacillus mucosus capsulatus* reported by many other investigators. Castellani and Mendelson[11] report the isolation of an encapsulated bacillus belonging to the group *B. lactis aerogenes, genus encapsulatus*, from most of the cases of granuloma inguinale studied by them. They are, however, quite skeptical of the evidence that this organism is the cause of the disease because the inoculation of such cultures into animals produces only purulent lesions which are not in any way comparable to those of granuloma inguinale. McIntosh[9] has reported the successful transmission of the disease from one person to another by tissue transplantation, but no one has reported the successful infection of laboratory animals by any method.

During the past fifteen months we have made cultures from six cases of granuloma inguinale at the Vanderbilt University Hospital, and from the fresh tissue of an additional case sent us from Memphis.* All of these cases occurred in negroes. Because of their similarity, the results of the studies of six of these seven cases can be reported collectively and very briefly. Typical Donovan organisms were present in smears from all of the lesions. Direct tissue inoculations into monkeys (*Macacus rhesus*) and other laboratory animals failed to produce the disease. Scrapings and tissue, repeatedly washed in physiological saline solution, were used in the cultural experiments. In addition to the ordinary culture media special media of various kinds were used. These included Sabouraud's medium, blood agar plates (using both human and rabbit's blood), agar and blood plates smeared with concentrated human leucocytes, including those from the specific cases under study, agar plates to which fresh egg yolk in ascitic fluid has been

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*From the Department of Pathology, Vanderbilt University Medical School.

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We are indebted to Dr. H. C. Schmeisser, of Memphis, for this tissue. Dr. F. M. Johns, of New Orleans, also assisted us in getting tissue from several other cases.

added, yeast extract agar, Dorsett's egg medium, Petroff's medium, Loeffler's blood serum medium, Francis' cystine agar, yeast broth, dextrose broth, patient's serum both active and inactivated, patient's and other human leucocytes added to patient's serum, to broth, and to ascitic fluid, fresh rabbit's spleen and liver added to broth and to the patient's serum, fresh egg yolk added to broth, to ascitic fluid and to the patient's serum. Cultures on these media were carried out aerobically and anaerobically, at both incubator and room temperatures. In none of these cultures did we succeed in growing an organism of the mucosus capsulatus group, or any other organism possessing the morphological characteristics of the capsulated Donovan organism as it appears in smears stained by Wright's method. Neither did we cultivate uniformly any particular gram-negative organism from all of the cases. We did succeed in growing from the last three of these cases a gram-negative strepto-bacillus of variable morphology, which in several respects differed from the bacillus of Ducrey. This organism was grown in the patients' inactivated sera, but always in association with a streptococcus. It was found to grow best in ascitic fluid to which fresh egg yolk had been added. We were not able to devise a solid

Plate I

EXPLANATION OF PLATE I*

Fig. 1.—Ulcerative lesions in left inguinal region as they appeared when patient came under our observation. The swelling below and lateral to the large ulcer was later aspirated and material rich in Donovan organisms and free from secondary bacteria was obtained.

Fig. 2.—The ulcers as they appeared two weeks after aspiration of the new lesion.

Fig. 3.—Ulcerative lesion on posterior aspect of left shoulder.

medium on which this organism would grow. Nor were we able to separate it from the streptococcus by dilution of subcultures. Other organisms recovered from the lesions included staphylococci of various strains, streptococci, diphtheroids, and from two cases a streptothrix.

Animals inoculated with these microorganisms failed to develop lesions similar to those of granuloma inguinale. But in spite of this failure to induce the disease in animals we continued tentatively to regard the strepto-bacillus as the causative agent of the disease until we failed to cultivate it from our most recent case which we now report.

H. Y., a negro man 27 years of age, was admitted to the surgical service of the Vanderbilt University Hospital on September 19, 1930. He complained of sores on his left hip. Thirteen months previously he developed a urethral discharge with burning upon urination. Immediately thereafter, a small ulcer appeared on the prepuce. This was followed by painful swellings in both inguinal regions. Two months later these swellings broke down. The patient was hospitalized for a period of five months, during which time the inguinal lesions were curetted. A diagnosis of granuloma inguinale of three months' standing was made. He was given daily 1 c. c. of 1 per cent tartar emetic intravenously for fourteen doses, but only slight improvement followed this treatment. We first saw him about eight months after the tartar emetic was discontinued. We found that there were small ulcerated areas at the upper edges of the old inguinal scars on either side. Also there were two granulomatous ulcers in the left groin. The larger of these ulcers measured 4x3 cm.; the smaller 1.5x1.0 cm. Their surfaces consisted of granulation tissue covered with a grayish, sero-purulent exudate. The granulation tissue projected above the level of the taut, heavily pigmented, surrounding skin. These ulcers bled easily, and they exuded a copious amount of serum. They were not very painful. The patient stated that the larger ulcer began as a boil about two months previously. Two weeks later it ruptured and a considerable amount of bloody material was discharged. The smaller ulcer developed in the same manner, but had existed for only two weeks. On the posterior aspect of the left shoulder there was a similar ulcer measuring 2.5x2.0 cm. which had been present for three weeks. In addition the patient had a chronic cervical adenitis which was probably tuberculous in origin. His urine constantly contained numerous red blood cells and pus cells, but in spite of repeated examinations acid-fast bacilli could not be demonstrated in the urine. Frequently he complained of pain in the region of the right kidney. Upon these findings a diagnosis of cystitis was made. The white blood cells varied from 10,000 to 14,000 with the differential count showing nothing remarkable. The Wassermann and Kahn reactions of the blood were negative. He was quite anemic and his poor general condition was, no doubt, at least partially responsible for the poor resistance offered to the granuloma inguinale infection. Smears from both the inguinal and shoulder lesions were extremely rich in encapsulated and non-encapsulated Donovan organisms.

While the cultural studies were being made on this patient he was kept in bed and given only symptomatic treatment. The lesions were cleansed and dressed daily, but the use of strong antiseptic solutions was carefully avoided. We were fortunate enough to observe the formation of two unruptured lesions near the ulcers in the left inguinal region. These unruptured lesions were aspirated and approximately 1 c. c. of thick pus was removed from each. Smears of this pus showed large numbers of mononuclear cells containing both encapsulated and non-encapsulated forms of Donovan organisms, which to all appearances were as healthy as those occurring in the cells of the ulcers.

The aspirated material was planted in the wide variety of culture media used in the study of the other cases. In addition, Noguchi's medium for leptospira was employed. The incubations were carried out aerobically and anaerobically at both incubator (37° C.) and room temperatures (about 22° C.). Some of the cultures were sealed and examined five weeks later. The inoculum proved to be free from contamination by other organisms. In the liquid media the Donovan organisms were followed to disintegration, which was usually complete after five days. The only suggestion of growth occurred in the patient's serum. Smears from this culture showed a few elongated, non-encapsulated organisms rich in chromatic material, and similar in appearance to long bacillary forms which we have occasionally seen in cysts within the mononuclear cells of the human lesion. Actual growth of the organism, if present, could not be maintained in subcultures in the same or other mediums.

Tissue removed from the lesions and thoroughly washed in 0.85 per cent saline still contained large numbers of Donovan organisms. In several instances pieces of tissue were almost entirely freed of contaminants by washing in saline, staphylococci not becoming noticeable in the liquid cultures until the fourth day. Tissue was also completely rid of contaminants by put-

EXPLANATION OF PLATE II*

Fig. 1.—Polymorphonuclear leucocyte, containing Donovan organisms.

Fig. 2.—Polymorphonuclear leucocyte, containing Donovan organisms in cystic formation.

Fig. 3.—Immature mononuclear cell which is infected by Donovan organisms.

Fig. 4.—Immature mononuclear cell which contains many encapsulated Donovan organisms.

Fig. 5.—A large mononuclear cell which contains a single small cyst filled with non-encapsulated forms of Donovan organisms.

Fig. 6.—A large mononuclear cell which contains non-encapsulated forms of Donovan organisms.

Fig. 7.—A mononuclear cell filled with large encapsulated Donovan organisms.

Fig. 8.—A large mononuclear cell which contains two cysts. The cyst above the nucleus contains non-encapsulated forms; the one to the right of the nucleus contains encapsulated forms.

Fig. 9.—A large mononuclear cell in which the organisms within the cysts seem to be dividing (longitudinal fission).

*All photo-micrographs represent magnification X2300. Unless otherwise specified all microscopic preparations are stained by Wright's method.

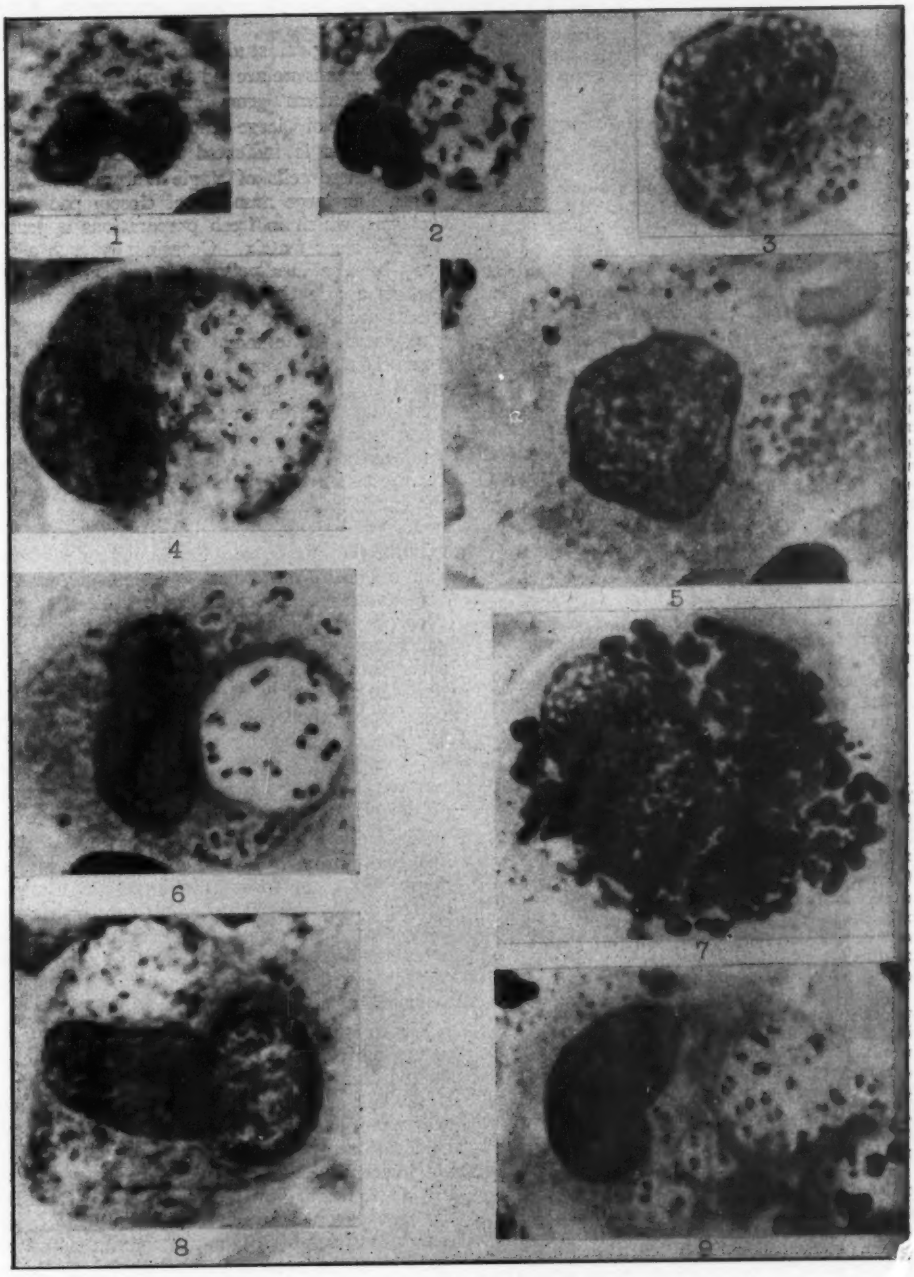

Plate II

ting small pieces in Dakin's solution for thirty minutes. It is believed that many of the intracellular organisms survived this treatment. Large forms of Donovan organisms developed in cultures of this treated tissue, but we could not obtain growth in subcultures.

The Donovan organisms persisted longest in those liquid cultures which had the least growth of contaminants. For the most part the organisms were seen to maintain their characteristic grouping within the disintegrating cells, and soon showed signs of disintegration as indicated by their loss of chromatin and by their pink-staining qualities with Wright's stain. In broth cultures to which fresh rabbit's spleen had been added some of the organisms were more persistent. They became three to four times as large as the usual forms and maintained their well-defined capsules. The chromatic material became increased in amount, stained more intensely, and apparently assumed a bipolar arrangement. It was found that the organisms persisted much longer if the cultures were kept in an atmosphere of carbon dioxide at room temperature. Rabbit's bone marrow, human leucocytes, and human spleen were substituted for the rabbit's spleen, but no evidence of actual multiplication of the organisms could be obtained, although subcultures were attempted at frequent intervals. The organisms assumed their largest size in the patient's citrated plasma, which was collected and maintained in an atmosphere of carbon dioxide. In some of the cultures these large forms were observed for a period of fifteen days, and when they did begin to disintegrate they disappeared from the cultures within a few hours. These cultural studies are being continued.

The richness of the tissue from this case in Donovan organisms and the relatively slight contamination of it with secondary bacteria made it especially suitable for use in attempts to infect animals. Scrapings from the lesions were suspended in saline and inoculated subcutaneously into guinea pigs, rabbits, kittens, dogs, rats, and into four *Macacus rhesus* monkeys. All of these animals, excepting the monkeys, developed small localized abscesses in which no Donovan organisms persisted, but which were abundantly infected with cocci.

We were able to establish an infection by Donovan organisms in three of the four monkeys by repeated inoculations of the human material. Following injections of scrapings suspended in saline there was no obvious development of abscess. An area of induration occurred and persisted. In only one of the monkeys did a lesion, situated in the lower eyelid, ulcerate. This took place about three weeks after the first injection. Smears from the granulating surface showed numerous polymorphonuclear leucocytes and large mononuclear cells containing the Donovan organisms.

In another monkey Donovan organisms were found within mononuclear cells of a non-ulcerative lesion five weeks after the last injection. Smears have been made from non-ulcerative lesions by aspiration at intervals. We have found it easy to demonstrate infected cells by staining the smears by Gram's method as well as Wright's stain. For determining encapsulation the latter method has always been used. These animals are still under observation, and it is too early to determine whether or not a permanent lesion can be established. The tendency in each monkey at present is toward healing.

DISCUSSION

In cytological studies of the cells from the human lesions we are led to judge that the Donovan organisms grow extensively within the cytoplasm of large mononuclear phagocytic cells. This is indicated by the appearance within these cells of single and multiple cysts containing large numbers of closely packed organisms, which in fresh preparations appear to lie in a clear matrix. Occasionally such a cyst may be seen in a polymorphonuclear leucocyte, but as a rule the organisms in polymorphonuclears are few and scattered and usually unencapsulated. The mononuclear leucocytes apparently may become heavily infected while still much smaller than the large, obviously phagocytic stage. This we regard as an evidence of invasion and multiplication of the Donovan organisms in these cells, rather than as a simple manifestation of phagocytosis. The mature mononuclear cells may become infected by phagocytizing polymorphonuclear leucocytes which contain the organisms. Small groups of Donovan organisms of different sizes, and showing various stages of capsular development, have been observed within such phagocytized and degenerating polymorphonuclear leucocytes. In such instances some of the forms are so small that the possibility of their being filterable is suggested, although McIntosh was unable to infect a human subject with filtered material from a lesion. When the infected cells are stained supravitally, they present the staining reactions of the clasmatocytic type of cell.

The basis on which we judge that an infection has been established in monkeys is the great number of Donovan organisms present in mononuclear cells within the lesions, and especially their arrangement in cysts corresponding in every way to those of the human cells. The presence of intracytoplasmic cysts is interpreted to mean intracelluar multiplication.

We are convinced that the Donovan organism occurs both in an encapsulated and non-encapsulated form within the large mononuclear cells of the human lesions. A single cell may show one cyst filled with the typical encapsulated Donovan organisms, and another cyst containing unencapsulated organisms in every respect similar to those in the first cyst, except for the absence of capsules. Occasionally, intracellular cysts have been found to contain elongated bacillary forms, which we also regard as Donovan organisms, and short forms which present evidence of longitudinal fission. It appears to

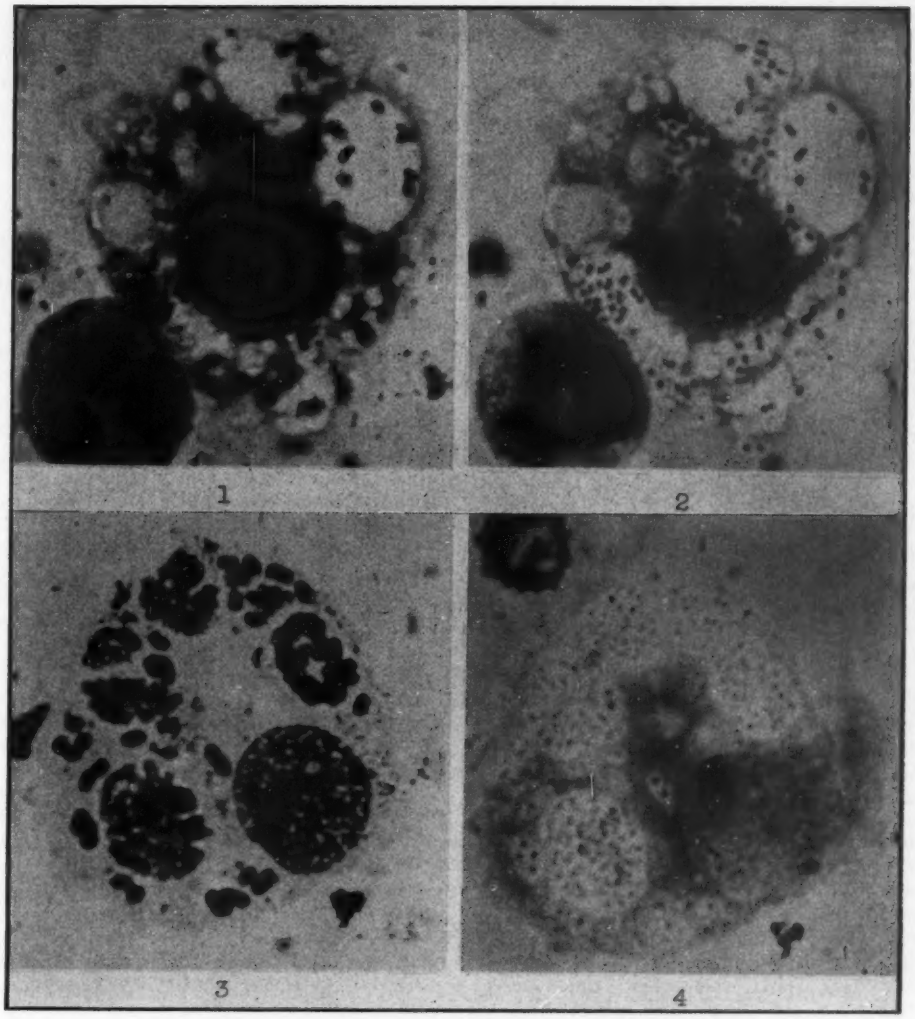

Plate III

EXPLANATION OF PLATE III*

Fig. 1.—Mononuclear cells in which both encapsulated and non-encapsulated forms of Donovan organisms occur in the same cyst.

Fig. 2.—Same cell as presented in Fig. 1 after decolorization with acid alcohol and stained by Gram's method.

Fig. 3.—Mononuclear cell containing multiple cysts filled with encapsulated Donovan organisms.

Fig. 4.—Same cell as presented in Fig. 3 after decolorization with acid alcohol and stained by Gram's method. Capsules are not demonstrated.

us that this infectious agent is variable in its morphology, and may be bacterial in nature. Evidence for this is to be found also in changes which may take place in individual Donovan organisms in culture media. So far as our observations go, the Donovan organism seems to be a facultative or obligate intracellular parasite, although there are some indications that under suitable conditions it might reproduce extracellularly.

It is inferred that within the human lesion the organisms are continually being liberated by the rupture of the large mononuclear cells. The liberated organisms are free to infect other cells. The presence of minute, focal accumulations of polymorphonuclear leucocytes in histological sections of the lesions may be explained as resulting from the action of an injurious material liberated along with the organisms, or upon their disintegration. The constant proliferation of granulation tissue may be likewise explained.

The establishment of an infection in monkeys offers for the first time a means of testing biologically without the use of a human being any microorganism which may be grown from the lesion and suspected of having an etiological relationship. The Donovan organism, if cultivated, should, like the inoculated human tissue, induce lesions in monkeys characterized by encysted groups of these microorganisms within large mononuclear cells.

In comparing the results of our cultural studies with those of other investigators as recorded in the literature, we are impressed with the fact that comparatively few Gram-negative bacilli occurred in the lesions studied by us. Possibly contaminants, including members of the *Bacillus mucosus capsulatus* group, occur with greater frequency in cases in the tropics. The contaminants which we encountered most often were staphylococci of various strains, streptococci, and diphtheroids.

Since the Donovan organism is Gram-negative, most of our studies were concerned with Gram-negative organisms; although we also inoculated into animals all Gram-positive organisms which were, on account of their morphology or the frequency with which they occurred in the lesions, in the least suspicious.

Until we had the opportunity of studying our last case we thought that our failure to cultivate the Donovan organism was probably due entirely to the inhibiting influences of secondary organisms. Since our failure to cultivate the organism from uncontaminated material, we conclude that it cannot be cultivated by any of the ordinary methods, and that for its successful cultivation special methods must be devised.

We attribute our success in infecting monkeys with Donovan organisms by repeated inoculation to the fact that the human material injected was extremely rich in Donovan organisms and contained relatively few secondary bacteria.

We are thus made aware of a biological test, employing laboratory animals, which may be carried out with any organism recovered from the lesions and suspected of being the etiological agent of the disease.

SUMMARY

(1) The results of cultural and cytological studies of seven cases of granuloma inguinale are reported.

(2) In none of our cultures did we succeed in growing organisms possessing the morphological and staining characteristics of the Donovan organism.

(3) From one of the cases there was obtained for cultural purposes material rich in Donovan organisms and free from secondary bacteria. From culture of this material no evidence was obtained that the Donovan organisms increased in numbers.

EXPLANATION OF PLATE IV*

Fig. 1.—Encapsulated Donovan organisms in tissue smear after tissue had been washed in twelve changes of 0.85 per cent saline.

Fig. 2.—Smear of washed tissue which had remained 24 hours in broth containing fresh rabbit's spleen. Note both encapsulated and non-encapsulated forms.

Fig. 3.—Long form of Donovan organism which occurred in broth containing human leucocytes after remaining five days in carbon dioxide at room temperature (Gram's stain). This organism showed a well defined capsule when stained by Wright's method.

Fig. 4.—Other forms of Donovan organisms which occurred in the same preparation as Fig. 3.

Fig. 5.—Group of enlarged Donovan organisms in a smear taken from a 48-hour culture of inguinal tissue in yeast broth.

Fig. 6.—Donovan organisms in smear form a 24-hour subculture of inguinal tissue which had remained in yeast broth for 90 hours. Some of the forms are greatly enlarged; others are of the size encountered in fresh smears from the human lesions.

Fig. 7.—A smear showing one of the long bacillary forms which occurred after 90 hours in a culture of the uncontaminated pus planted in the patient's serum.

Fig. 8.—A large mononuclear cell from a human lesion showing a cyst which contains long bacillary forms of Donovan organisms.

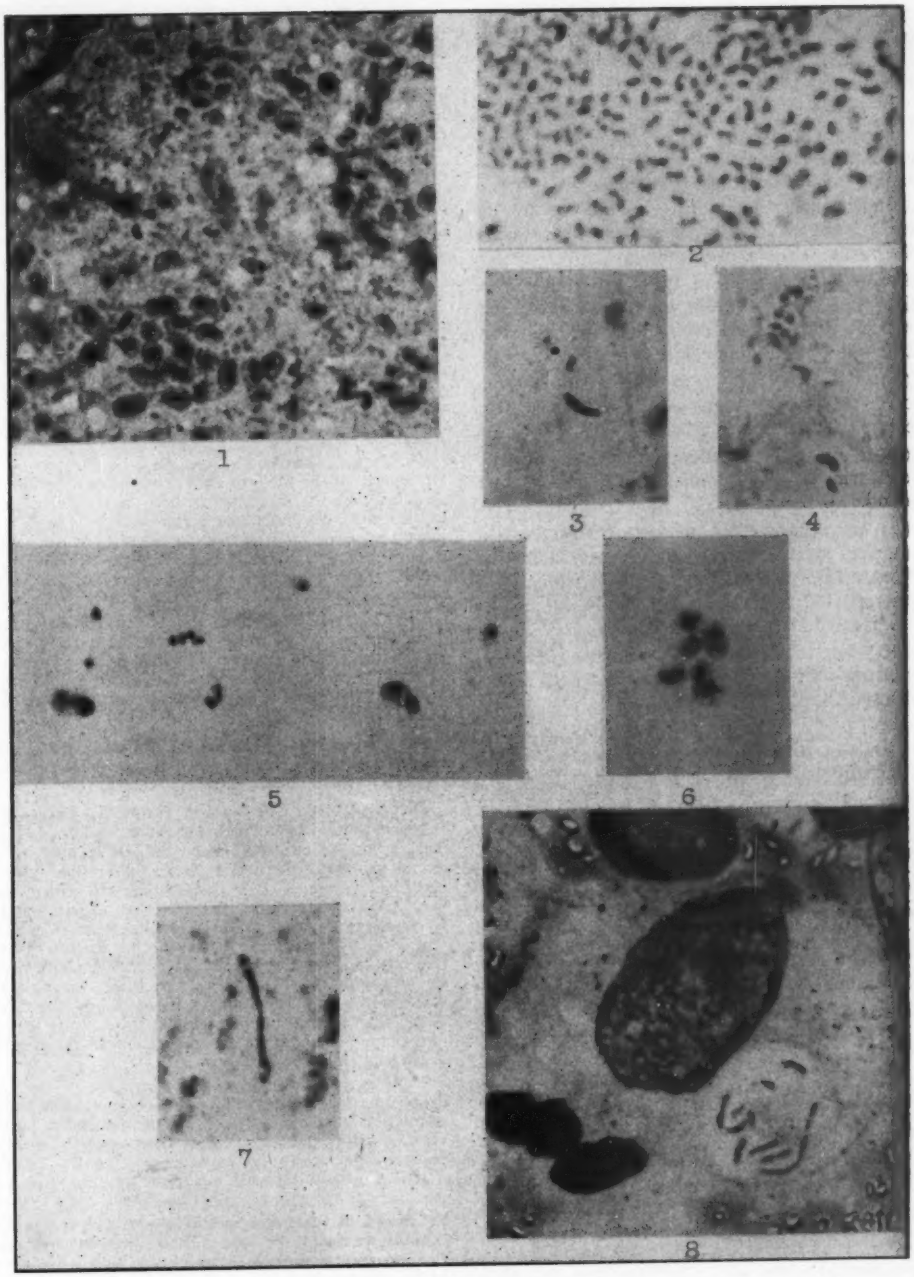

Plate IV

(4) There is evidence that Donovan organisms may increase in size and remain viable in cultures free from contamination for a considerable period of time.

(5) Based upon the presumptive evidence derived from a study of the morphology and staining characteristics of the organism, and developmental changes which take place in it when suspended in certain culture media, we are inclined to regard this organism as a parasitic plant rather than a protozoan.

(6) Upon the basis of cytological studies we judge that multiplication of the Donovan organisms within human lesions takes place mainly within the large mononuclear cells.

(7) The Donovan organism occurs in both encapsulated and non-encapsulated forms within the large mononuclear cells.

(8) Neither encapsulated nor non-encapsulated forms of the organism stain by Gram's method.

(9) We regard the Donovan organism as the etiological agent of granuloma inguinale; and we judge that none of the organisms which have been reported as cultivated from the human lesions is responsible for the disease.

(10) For the first time animals (*Macacus rhesus* monkeys) have been infected with Donovan organisms.

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DISCUSSION (*Abstract*)

Dr. J. A. McIntosh, Memphis, Tenn.—We have tried the passage of human material of this kind obtained by biopsy into one monkey. The monkey did not develop the characteristic lesion at the site of the graft.

I have never seen this disease in the white race. I should like to ask Dr. DeMonbreun whether his cases occurred among negroes.

I believe that the Donovan body is the cause of granuloma inguinale, as Dr. DeMonbreun believes. It has been cultivated, but I think convincing proof of cultivation is lacking.

Superficial scrapings from the surface of the ulcers do not yield the Donovan bodies. Aspirated juices from deeper portions generally contain them. We have found that the distance which the organisms maintain from one another is helpful in locating them in the microscopic field. Invariably you find the characteristic cyst-like collection of the organisms in the mononuclear cell. From my observation I did not think the polymorphonuclear phagocytized the bodies. However, the doctor has shown some photographs indicating that they do. The mononuclear cell possesses a greater selective action for this parasite.

The powerful effect of tartar emetic on the lesion is noteworthy. I have yet to see a lesion which will not disappear under antimony injections.

Dr. Jack C. Norris, Atlanta, Ga.—In 1919 or 1920, Dr. Lynch, of the Medical College of the State of South Carolina, won the American Medical Association's medal for his work on granuloma inguinale. Dr. Lynch isolated organisms from granuloma ulcerations and with a pure culture produced lesions on the abdomens of rabbits which resembled to some extent the lesions of granuloma inguinale.

Dr. Mood, of Charleston, and I, working on granuloma inguinale, were able to culture similar organisms on Loeffler's blood serum. They had so many characteristics of diphtheroids that we experimented with antitoxin as a curative agent, but of course without any results.

Dr. Charles Phillips, Richmond, Va.—Did the clinical course of these patients include any mononuclear changes in their blood?

Dr. Ernest W. Goodpasture, Nashville, Tenn.—The last case which Dr. DeMonbreun reported, I think, is as ideal a case as one could hope to find in a study of granuloma inguinale, which is an ulcerative disease and highly contaminated. In addition, the patient had very poor resistance to the infection. Consequently, it served as an ideal means for cultural investigation; and Dr. DeMonbreun was on the wrong track until this case came up, because of the persistent Gram-negative organism which came out in three other cases. The study is important among other things in emphasizing the necessity of examining many cases before one commits himself as to the etiological relationship of any organism to a disease.

I am convinced, from what I have seen of Dr. DeMonbreun's work, that the cause of granuloma inguinale is the Donovan body. From the number of media, the care with which he selected them, and the quality, he is convincing, so far as I am concerned, that the granuloma organism will not grow on any ordinary medium.

I was also impressed by the appearance the organisms presented in the mononuclear cells, in such relationship and under such circumstances, that they appear to be cytotropic microorganisms. I think all the different forms, encapsulated and unencapsulated, are the same microorganism. The evidence, too, while cer-

tainly not conclusive, seems to me to be in favor of the view that this is a plant parasite rather than an animal parasite. It seems that the organism proliferates entirely intracellularly.

It is very important that Dr. DeMonbreun has been able to produce similar changes in monkeys. It is probable that the experimental lesions will not develop into chronic granulating lesions, but the appearance indicates that the Donovan organism is growing in the mononuclear cells, judging from the great numbers which are in the cysts. There is no other organism I know of that will produce that appearance. Consequently I think we have a means here of identifying the Donovan organism, if it should be artificially cultured, without resort to the inoculation of human beings.

Dr. DeMonbreun (closing).—All of our cases occurred in negroes, most of them in negro women.

I read Dr. Lynch's paper, which appeared in the *Journal of the American Medical Association* in September, 1921. As I recall, in that article he describes a Gram-negative bacillus with which, so far as I have been able to make out, he has not been able to produce the infection in animals.

We have come across diphtheroids in several of these cases and have tried cultures of these diphtheroids in various animals and have not succeeded in producing any changes in the cells similar to those caused by the Donovan organism. We feel fairly positive that the Donovan body is a Gram-negative organism. The diphtheroids we found have all been Gram-positive. That is another thing that we believe rules out the diphtheria group.

We have made differential counts on almost all of these patients and have not found that the mononuclears are increased.

CAPUT OBSTIPUM CONGENITUM*

By LUTHER W. HOLLOWAY, M.D.,
Jacksonville, Fla.

My interest in this subject was aroused four years ago, when I had occasion to see a little patient, three weeks of age, in whom the mother had discovered a tumor, which had appeared rather suddenly in the right side of his neck. The antenatal and birth history were negative as far as trauma by instruments or any difficulty in delivery was concerned. The mother stated that the baby had been fussy, and had not nursed well for three or four days before she consulted me. The child rested better on the right side. Upon examination, there was found a hard, solid mass the size of a pigeon's egg in the substance of the right sternomastoid muscle. It occupied a position about the junction of the middle and lower thirds and was movable with the muscle. There was no apparent tenderness. The head was inclined to the right side. I did not know what the condition was, so observed the baby for two weeks, during which time the mass increased in size. Fearing that the condition was malignant, surgical consultation was suggested. We wished to make the diagnosis by operation and tissue study. At operation a hard mass was found, which involved only the muscle. This was removed, and it measured ¾ inch in thickness and 1¾ inches in length. It involved three-fourths the diameter of the muscle. It was greyish in color, firm in consistency, and resistant to the blade. Microscopic study revealed a replacement of practically all of the muscle by fibrous tissue. Four years later, the patient presents a normal appearance.

Two years elapsed before a similar condition again came under my observation. In the last two years, ten cases of like nature have been encountered by my confreres and myself.

The etiology of this condition, found in the sternocleidomastoid muscle of the newly born, and its relationship to torticollis, has never been actually determined. Many interesting theories have been advanced, but none has been accepted as final.

Mikulicz[1] believed that caput obstipum was a result of myositis fibrosa and that the myositis, in most cases, is due to contusion of the muscle against the symphysis or ligamentum arcuatum during labor.

Kader[1] was of the opinion that following birth trauma there developed a myositis which was of hematogenous or intestinal origin.

Such authorities as Koster, Milo, Pincus, Kehrer and Rettig[1] believed that the muscular changes had begun *in utero*, and that these intrauterine changes in the sternomastoid muscle, described as fibro-myositis, dystrophy, or developmental disturbances, are certainly not yet explained.

Durante[1] mentioned syphilis as a cause, but no positive tests have been found, nor have there been any of the typical symptoms of lues in the patients examined.

Peterson[1] believed that congenital wry-neck could be caused by adhesions between the fetus and the amnion.

Voelker[1] described caput obstipum congenitum as an intrauterine hereditary deformity. When the amount of amniotic fluid is not sufficient, the elastic pressure of the uterine walls causes lateral flexion of the head. In this way the shoulder is placed in a cavity formed between the mandible and the clavicle in the middle of which the vessels are situated, and are firmly compressed by the shoulder against the middle of the vertebral column.

"Should this pressure persist, there is an interference to the supply of arterial blood and venous congestion takes place. In this way a slow, fibrous degeneration, after an originally spindle-shaped swelling, takes place below the middle of the muscle. Finally, the sternomastoid muscle on one side of the neck is represented by a shortened, hard strand; the head is bent sideways, and, as a rule, its perpendicular axis is somewhat displaced."

A. Stern,[2] in 1924, reported a case which bears out the above idea of Voelker. The patient, a complete breech presentation, was delivered by cesarean section after 48 hours of labor. Stern said the head was inclined 45 degrees to the left and at the same time was displaced, as a whole, somewhat to the right. The

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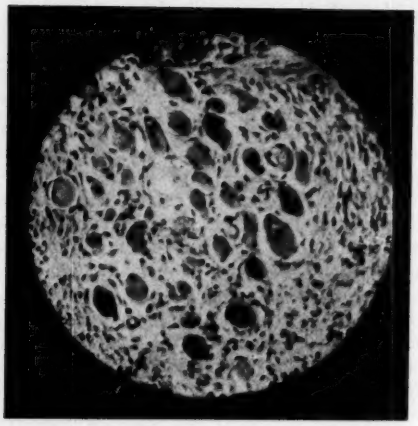

Fig. 1
Section of tumor mass noticed three days after birth and excised nine days later (X300). Shows replacement of muscle fibers by fibrous tissue.

left shoulder, which was lifted high, had pressed a deep indentation in the slightly atrophic musculature of the left side of the neck.

"Muscular injury may be incurred in either spontaneous or artificial delivery. By tearing and stretching, muscle fibers may be ruptured in varying degree. In this way intramuscular hemorrhage may occur. According to Mikulicz, injury is especially liable to occur in muscles in a contracted condition, when affected by the traumatic agency. Kader says that the respiratory muscles are endangered by premature respiratory movement."

"According to Schauta,[1] breech presentations are responsible for more injuries to the sternomastoid muscle than any other type. They occur when the shoulder is in the sagittal diameter of the pelvis while the head is placed in the same diameter of the pelvic inlet, or in head presentations, in which the head is already rotated in the pelvic floor, and the shoulders are still in a sagittal plane. In both instances, the head has undergone a right-angled turn from the body."

The theory of Stromeyer[2] is that the congenital torticollis is usually caused by rupture of the muscle and by myositis about the hematoma that may involve and ultimately destroy a large part of the muscle, replacing it with fibrous tissue, which, contracting, causes deformity. Whitman[3] challenges this theory as follows:

(1) Such changes do not take place elsewhere in the body.

(2) Heller says that myositis and contraction cannot be produced in the muscles of experimental animals, unless accompanied by pyogenic infection.

(3) In his 55 cases of supposedly congenital torticollis, seven gave a history of birth injury. Two of the seven had hematoma in addition to congenital shortening of the muscle.

(4) Cases of hematoma, as a rule, are not followed by wry-neck.

(5) In certain cases, a congenitally shortened muscle may be ruptured at birth.

(6) There are many other causes of tumors in the sternomastoid than birth injury, particularly syphilis and sarcoma. Whitman has collected from the whole literature 16 cases in which the muscle was practically replaced by cartilaginous tissue.

Koster suggests that on account of wry-neck, the fetus does not fit into the genital canal, so that in these cases the caput obstipum may not be the result, but the cause of breech presentations. From the above he concludes that in the sternomastoid of the newly born there are two kinds of changes:

(1) Ruptures and hemorrhages caused by birth injuries, which usually heal with simple scar formation, not interfering with function, nor tending to lead to permanent wry-neck.

(2) Changes beginning *in utero*, therefore congenital, and probably independent of birth injury, which give rise to the condition of wry-neck.

Brooks[4] has furnished some interesting data as a result of experiments upon isolated muscles. He has shown experimentally that ligation of the venous system causes marked changes in the muscle, which ultimately lead to muscle destruction followed by mass fibrous replacement.

Stewart Middleton[5] has just reported his work, in which he repeated Brooks' experiments on thirty dogs, using the sartorious muscle. His conclusions are the same as Brooks'. When he removed the sartorious muscles eight weeks after ligating their venous supply, he found a pathological picture which appeared to be almost identical with that revealed by tissue removed from the sternomastoid muscles in six weeks old infants who had had caput obstipum.

D'Arcy Power,[6] in an exhaustive study of wry-neck and congenital hematoma of the sternomastoid muscle thirty-seven years ago, collected from the literature 106 cases. In his analysis of this series he found that there occurred 21 cases of well marked wry-neck. In a series of 30 cases observed by himself and

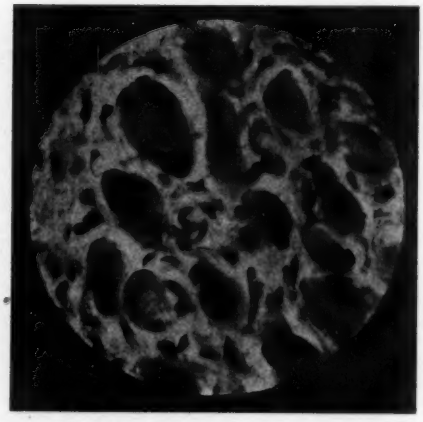

Fig. 2
Same as Fig. 1 (X600).

Fig. 3
Section of tumor mass discovered two weeks after birth and excised three weeks later (X300). Thrombus formation in addition to fibrous changes.

immediate associates, eleven cases of torticollis are reported. These cases were of varying degrees of severity. He reports no asymmetry of the face. Four cases were severe enough to require tenotomy.

Bilton Pollard[7] reported, in 1896, that among 23 cases of sternomastoid tumors, which he observed over a period of three years, 17 were cephalic presentations. This finding is not in accord with the belief that a majority of these tumors are found in cases which were breech deliveries. In two cases upon which he operated for torticollis, the affected muscle had been the seat of a hard swelling, which gradually disappeared in the first few months of life.

Jones and Lovett[8] have observed wry-neck following tumor of the sternomastoid muscle. One case cited had a difficult delivery. It was seen a few days after birth and had an unmistakable tumor of the muscle. Two years later definite wry-neck was present.

I submit for your consideration a brief summary of our cases to date.

(1) The time of discovery of the mass varied from three days to seven weeks, the average time being two weeks.

(2) The mother or nurse usually finds the mass.

Only one out of eleven cases was found by the physician, and this was found by Dr. Jelks, of Riverside Hospital, on the third day. This child had a congenital wry-neck, which was marked at birth. There was present also perceptible asymmetry of the face. Both feet were in a state of marked dorso-flexion. This baby was operated upon on the twelfth day, with excision of the mass. At ten months, the child presents a practically normal appearance.

(3) Six cases occurred in males and five cases in females.

(4) Seven cases were cephalic presentations. Two of these were delivered by low forceps, five normally.

(5) One 5.5 pound boy was delivered by cesarean section. The tumor was noticed on the twelfth day.

(6) One version was performed in this series, and there was one breech delivery.

(7) The position was diagnosed in six cases before delivery. It was left occipital anterior in 3 cases, right occipital anterior in 1, right occipital posterior in 1, and breech in 1.

(8) The muscle on the right side was affected six times, and on the left side five times.

(9) Two cases showed foot anomalies, namely, acute dorso-flexion.

(10) One patient was a negro. This patient, in addition to the tumor mass, has had since birth an inspiratory squeak and wheezing. X-ray study showed a markedly enlarged mediastinal shadow.

(11) Five cases were operated upon with removal of the tumor mass. Of these, one at seven months shows a slight tilting of the head towards the affected side, while the remaining four are apparently normal. Six cases had no treatment. In four of these the tumor has disappeared without leaving any apparent disfigurement. Two cases, however, at sixteen and eighteen months, respectively, both girls, have obvious wry-neck, with appreciable asymmetry of the face. In these two children the muscle is represented by a fibrous cord one-fifth to one-sixth the diameter of the muscle.

Fig. 4
Same as Fig. 3 (X600).

Fig. 5
Section of tumor mass seen two weeks after birth and excised five weeks later (X150). Shows later stage and more marked fibrosis than Figs. 1 and 3.

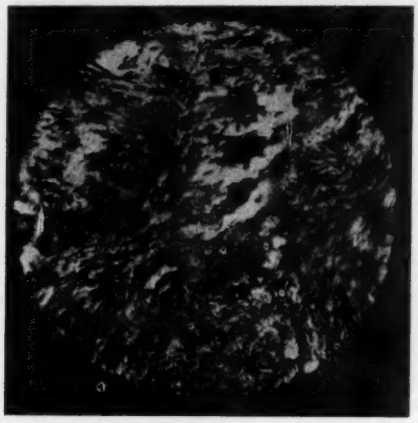

Fig. 6
Same as Fig. 5 (X300).

The pathological findings demonstrated in the removed tissue have been the same in the five cases studied, namely, a replacement of the muscular substance by fibrous tissue. No blood pigment was demonstrated in any of the sections.

TREATMENT

Most authorities advocate no treatment until the patient has reached the age of four years, expecting a spontaneous cure. Some merely suggest massage and exercise.

Rosenbaum,[9] this year, reports the cure of nine cases of sternomastoid tumor by repeated injections of 1 per cent solution of pepsinum purissinum in Pregl's iodine solution, according to the formula of Payr.

When one realizes that the pathology is that of destruction and replacement of muscles by non-yielding fibrous tissue, and that this tissue will not relax nor stretch, but has a tendency to shorten as time goes on, it seems hardly logical for one to expect a lengthening of the replaced sternomastoid muscle by time alone, or by forceful stretchings, which, if sufficiently carried out, will have the effect of stimulating further development of scar tissue.

Although our series is a very small one, the results which obtain from early excision convince us that early surgical interference should be employed more frequently in the future than it has been in the past.

CONCLUSIONS

(1) Caput obstipum of the sternomastoid muscle is a clinical entity and is not a hematoma.

(2) Caput obstipum is usually followed by wry-neck.

(3) Caput obstipum should be treated actively and not expectantly.

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DISCUSSION (*Abstract*)

Dr. Edward Jelks, Jacksonville, Fla.—Of course the line of treatment in these cases depends upon both the pathological findings first observed and upon what may be expected to develop as the patient grows older. It is disappointing to find in the literature little information as to what may develop later in these children, and also little knowledge of the exact pathological condition.

It is thought by some that the condition will develop into wry-neck. Others are of the opinion that these lumps in the neck are simply hematomas caused by injury to the muscle during birth or *in utero*.

I wish we had the opportunity in Jacksonville to do some experimental work on fibrosis in muscles. We are familiar with the work of Dr. Brooks, published in 1922, wherein he brought out the fact that if the blood supply of the muscle be cut off the muscle will

first go through a stage of swelling and then be replaced by fibrous tissue. Dr. Middleton, of Edinburgh, has selected some 60 odd cases of unquestioned wry-neck where there had been a tumor in the sternomastoid muscle in children ranging from the ages of four weeks to eight years. He found the process of fibrosis of children eight years old to be apparently identical with the fibrosis he finds in patients where in earlier life there had been recognized a sternomastoid lump which later disappeared. He then experimented with dogs, as Dr. Holloway brought out in his paper, by cutting off the venous supply to the sartorius muscle. He found after the first two days that there was quite a congestion of the muscle with engorgement of blood which gave it the gross appearance of liver. After two days this engorgement stage cleared up and in a few weeks the muscle which had been enlarged returned to the same size as that of the other side, but it was then white in color, caused by a replacing of muscle fibers by fibrous tissue. The sections he took from the sartorius muscle of his experimental animals corresponded in appearance to the sections he removed from the sterno muscle of children at corresponding stages of the process. In both instances he demonstrated that there was the period of swelling from congestion followed by a period of contraction with fibrosis.

If, then, the so-called hematoma of the sternomastoid muscle is going to result in a destruction of that muscle with the consequent contractions which we speak of as wry-neck, we must also take a more decisive attitude in the handling of this condition than we have done in the past, and not blindly hope that these swellings will be resolved without the deformities of sternomastoid contractions.

Dr. A. A. Shapiro, Louisville, Ky.—Of all the theories regarding the origin of wry-neck, the most plausible one seems to be fetal malposition, lateral flexion of the head, with torsion of the neck *in utero*, causing a disturbance in circulation of the branches of the superior thyroid artery, the latter having, comparatively speaking, little or no anastomosis with surrounding vessels. Such a theory would explain the partial distribution of the lesion and the absence of primary involvement of the surrounding parts.

The clinical and experimental work of Nove-Josser and Vianny has placed this theory on a reasonable basis. They have demonstrated that in every case of wry-neck they have examined the lumen of the sternomastoid artery was obliterated.

I do not believe that hematoma of the sternomastoid results in wry-neck; the hemorrhage is absorbed without contraction. The hematoma results from extension of the head with previous congenital shortening of the muscle. Torticollis may manifest itself clinically later in life, at six months to a year.

As to the treatment, I believe in early massage and overcorrection by means of orthopedic appliances. I do not believe I have mentioned the use of a felt pad collar around the neck, immediately following birth, in cases in newly born infants. In more severe cases, it is necessary to resort to myotomy and overcorrection by means of a plaster cast. The earlier the treatment the better the results, since secondary changes are avoided. Fraser recommends excision of the muscle-like cord at the age of one month.

Subcutaneous tenotomy is mentioned merely to be condemned.

Dr. John A. Foote, Washington, D. C.—This condition may be found whether the large or small venous radicles are involved in the injury. The opinion given in the text books that it should be treated passively and not actively, must be revised, in view of the literature that Dr. Holloway has collected.

There are congenital conditions in which we have wry-neck independent of this injury. It is important to remember that when we have a congenital wry-neck, additional injury may occur to the sternocleidomastoid muscle on the side affected because of the extra strain placed upon the congenitally shortened muscle in the process of delivery. Thus we may have not only rupture of the veins and of the muscle tissue, but also a congenital shortening of that muscle as well as a traumatic shortening.

Dr. Holloway (closing).—Middleton in his splendid study of this condition explains satisfactorily the reason for the late manifestation of wry-neck in these cases. He states that the growth of the neck and thorax is slow until the child is three and one-half to four years of age and at this time the neck and body attain a more rapid rate of growth. The shortened fibrosed muscle becomes apparent with a pulling of the head to one side.

PULMONARY TUBERCULOSIS AND PREGNANCY*

By R. A. WHITE, M.D.,
Asheville, N. C.

Norris, in his book, "Gynecological and Obstetrical Monographs,"[1] has thoroughly covered the subject of pregnancy and tuberculosis. One has but to read this particular monograph to familiarize himself with the opinions of most of the authorities upon this subject since 1854. I wish to commend his book and to acknowledge free use of his material and statistics in the preparation of this paper.

Having been engaged in a fairly active obstetrical practice for ten years in a health resort community, where the chest specialist is always available for consultation and advice, I have made certain observations and arrived at certain conclusions which, in the main, agree with the authorities. There are, however, a few points upon which I cannot entirely agree with the majority of observers, and there are certain other points upon which I wish to lay especial emphasis.

Statistics from a short series of cases are of no value. Individual case reports of tuberculous pregnant women, to be of value, must have

*Read in Section on Obstetrics, Southern Medical Association, Twenty-Fourth Annual Meeting, Louisville, Kentucky, November 11-14, 1930.

long follow-up notes, x-ray examinations, and so forth. It, therefore, seems feasible to limit my remarks to a general discussion of the subject.

The frequnecy with which tuberculous women become pregnant is especially notable in health resorts such as Asheville, and this frequency is commented upon in much of the literature. This effect has led many of the observers to conclude that persons affected with tuberculosis are unusually fruitful and have an increased sexual appetite. Numerous observations have been recorded to bear out this assertion. Sexual intercourse is often indulged in by those in whom the disease is far advanced. Two women have recently been under my care whose husbands have died of pulmonary tuberculosis before the babies were born. It is usual for the wives of tuberculous soldiers who are under treatment in the U. S. Government Hospital at Oteen to become pregnant as often as is compatible with the processes of nature. The causes for the increased sexual desire are probably the inactive life, high caloric diet and slightly elevated temperature. Whatever the cause may be, it is recognized as definite by those who treat the tuberculous, and it is believed by many of our men that the moderate gratification of this urge is benefcial to a selected number of patients. Physicians may sanction moderate indulgence where a husband or wife or both are affected, and even sanction marriage among couples affected with tuberculosis. If moderate indulgence is beneficial, overindulgence is by the same token injurious and the physician in charge should attempt to regulate the practice.

There seems to be no evidence that tuberculosis has any influence on conception, and we know that pregnancy among tuberculous women is extremely frequent. It is much more frequent among the ignorant and poor, probably because they do not have the knowledge of or the means to supply the contraceptive methods. The tuberculous married woman whose condition is such that she should not become pregnant should be told how to keep from becoming pregnant and she should be shown and equipped with a simple method, which permits as nearly as possible the normal gratification of marital relations. Many a woman has come to me seeking abortion who has been told by her physician that to have another child would probably cost her her life. We, as physicians, are not fulfilling our duties until we supply the information to make it possible for these patients to follow our advice. We should go further than this. Through social agencies, public health nurses, and so forth, we should bring in for instruction these poor and ignorant women who are every year or two bringing into existence a child: a child who, if he lives and the mother lives, is to be brought up in a tuberculous environment, to become infected and to become a menace to others. Statistics show that about 50 per cent of children born of tuberculous mothers die during the first year of life (Bridgman[2]) and that about 12,000 pregnant tuberculous women die annually (Bacon[3]). In this day of so-called preventive medicine, where is there a more fertile field? When preventive measures are properly carried out, the problem of dealing with the tuberculous pregnant woman will be greatly lessened.

I know of no more disputed problem in medicine than that of the effect of tuberculosis upon pregnancy and the method of dealing with this complication. In studying the literature, one is impressed with the necessity of handling each case individually. Not infrequently in our section, the chest man will sanction deliberate conception where the lesion is mild and has been quiescent for approximately two years. The period of two years seems to be a more or less generally accepted period of time to wait. Norris[4] says:

> "Occasionally, a case may occur in which the lesion is limited in extent and has been inactive for at least two years. Under such circumstances, if the patient is intelligent and able to avail herself with proper treatment and supervision and if she is especially desirous of having a child, conception is justifiable."

If pregnancy takes place, it is most important that the patient be constantly under supervision of a man especially trained in chest examinations so that the slightest changes in the condition of the chest may be detected. Occasionally, x-ray examinations are of the utmost importance. There seems as yet no way of determining even with the most careful preliminary studies, which cases will do well and which will do poorly. Much depends upon the way in which the patient endures the first eight or ten weeks of nausea and vomiting. I cannot too strongly emphasize the importance of proper care during the first three months. The weight lost during this time is hard to regain and the damage done to the chest is hard to overcome. If nausea is severe and vomiting frequent, the patient should be kept constantly in bed and the usual methods used to control the nausea and prevent dehydration. If the condition cannot be controlled at home, the patient should

be put in the hospital, where rectal feeding, hypodermoclysis or intravenous therapy can be used. Patients who survive this period with little or no loss of weight or signs of extension in the lung may be reasonably expected to withstand the remainder of pregnancy. All of these patients should be definitely limited in their activities and many of them kept in bed most of the nine months. When nausea and vomiting cannot be controlled, when loss of weight cannot be prevented or when a beginning flare-up is detected in the lungs, then pregnancy should be terminated, preferably not later than the twelfth week.

The distressing part of the problem is that the great majority of patients, for economic or domestic reasons, cannot or will not avail themselves of this rather drastic regime. Then arises the question of what should be done.

Practically all authorities emphasize the importance of diet, proper hygiene and expectant treatment, but little stress is laid upon the value of bed rest. If there is one outstanding reason, in addition to those of climate and altitude, for our section's being noted as a resort for the tuberculous, it is that most of the men in Asheville treat their sick patients in bed not twelve hours a day, but twenty-four, and not for one month, but for many months. If bed rest is necessary for the non-pregnant tuberculous patient, it is far more important for the pregnant woman. About eighteen months ago, a woman came to me in the early weeks of her third pregnancy showing suspicious chest symptoms. She was sent to a chest man who, after careful study, said:

"Whether you are pregnant or not, you should spend the next nine months in bed. If you spend the next nine months in bed, you will probably be able to go through pregnancy safely."

She did not adhere closely to the regime and miscarried at six months, probably fortunately. With a prolonged bed rest following the miscarriage, she is doing well.

The patient who comes to me during the early weeks or months of pregnancy, with suspicious or positive evidence of trouble in the lungs, is sent to a chest man for study. If she is found to have extensive involvement, even though inactive, or a small active lesion, the uterus is emptied at once. I believe, too, that in those who have tuberculous kidney or laryngeal involvement, pregnancy should be terminated. The tuberculous woman, however quiescent, small or inactive her lesion, has less resistance than the non-tuberculous patient. Therefore, any other complications such as nephritis, cardiac involvement, stomach or gall-bladder disease, or hyperthyroidism, should definitely influence us towards a decision to terminate pregnancy.

On the other hand, in the patient who is found to have a small quiescent lesion, an extremely early lesion, or only suspicious signs of chest involvement and no other complications, the indications are not so clearly defined. Many of the above mentioned factors must be considered. Is it her first pregnancy? Is she especially desirous of a child? Is she willing and able to carry out the rigid regime which may be necessary, even to spending some or nearly all the nine months in bed? Is she willing and able to submit to frequent chest examinations and x-rays if necessary? Is she willing and able to be hospitalized if need be during the vomiting period and again for delivery? Will it be possible for her to take a long period of rest following the birth of the child, leaving the care of the child entirely to some one else? If all or most of these questions can be answered in the affirmative, I believe that a great many of these patients can be taken safely through to term or near term. If most of these questions cannot be answered in the affirmative, then very few patients should be allowed to go beyond the third month. The diagnosis of tuberculosis is easy in the advanced stages, but is extremely difficult in the very early stages. We depend upon a chest man for this, and he in turn depends upon repeated clinical studies and stereoscopic x-ray films. In the study of these doubtful cases or, in fact, in the study of any case where a therapeutic abortion is being considered, it is our custom to obtain the joint opinion of two chest men before proceeding with the operation.

The diagnosis of pregnancy during the early weeks is not always easy, and, since the earlier pregnancy is terminated the better for the patient, it is of the utmost importance that this diagnosis be made early. The menstrual history cannot be depended upon, since many tuberculous women are irregular and miss one or several periods without significance. The symptoms of nausea and vomiting and other digestive disturbances are not diagnostic, because many women who are slightly toxic from the tuberculous infection may have these symptoms. I should like to call attention to two early indications. First, as early as the fifth or sixth

week there can be felt on the anterior wall of the uterus a soft spot which pits on pressure as does an edematous leg. This sign has been described, but I cannot recall the name of the author. The second is the test described by Bullock,[5] which in brief is as follows: In the pregnant woman an artificial acetonuria is found, after eight or nine hours of fasting following a meal rich in fat, while in the nonpregnant at least forty-eight hours are required to produce this condition. We have tried this test in only a short series of cases, about 15 in all, besides a few controls, but it bids fair to be of value.

When a decision is reached that pregnancy should be terminated, the methods to be used are important. During the first three months dilatation and curettage can usually be accomplished at one stage. If there is any doubt as to the thoroughness with which the uterus is emptied, it should be packed with gauze for twenty-four or forty-eight hours. After the third month, it is not usually wise to attempt the one-stage operation unless a vaginal hysterotomy is to be done. Norris and others advise this procedure, claiming that there is less loss of blood, less anesthetic, and less pain than from the two-stage operation. In the hands of a skillful surgeon, this is probably true; but unless it is properly done there are dangers and the condition of the cervix following the operation leaves much to be desired. The two-stage operation, on the other hand, does not usually require more than one anesthetic. The cervix can be dilated with a preliminary hypodermic of morphine sufficiently to permit packing with very little pain. It is my custom to use a fairly large soft rectal tube, ten or twelve inches of which are allowed to coil up in the uterus, then two strips of gauze are pushed in beside the tube. The tube and gauze are left in the uterus twelve, twenty-four or even forty-eight hours until pains are well established, then removed. If the patient's condition is good and there is not too much bleeding, she may be allowed to labor for a few hours. I have had patients who expelled the entire contents of the uterus a few hours after the packing was removed. The usual procedure, however, is that, soon after the removal of the packing, the patient is given an anesthetic, nitrous oxide and oxygen, the dilatation, if not sufficient, is completed, and the secundines are removed.

The interruption of pregnancy even in the early cases is not always beneficial. The literature is abundant *pro* and *con* on this phase of the subject. The combined statistics of 21 observers comprising nearly 1,000 cases show that 77 per cent of the women are benefited by the induction of abortion. The percentages range from 20 to 97. The degree of the benefit will depend greatly upon the after care the patient receives.

The question of sterilizing the tuberculous woman at the time of emptying the uterus is a mooted one, but the majority of observers feel that it is not usually justifiable. I feel that opening the abdomen for the purpose of sterilization *per se*, in a patient sick enough to justify therapeutic abortion, is not warranted.

It is rather generally agreed that emptying the uterus after the fifth month is of little or no value and may actually shorten the life of the patient. It is all-important that the women who are doing poorly at this stage be given every care, including diet, bed rest, sunshine, and freedom from worry. This care only the well-to-do and the more intelligent can or will afford. Hence, the reason why the poor or ignorant should not be allowed to reach this stage.

There are two lives to be considered during the last months of pregnancy, and when the condition of the mother is hopeless our efforts should be directed towards the well being of the child.

Polak and Mathews[6] state that mild cases going to term may be completed without causing alarm, while in advanced cases the labor may be long and tedious with many dangers to the mother, such as dyspnea, cough, hemoptysis, impending cardiac failure, pulmonary edema, pneumothorax, and, rarely, general dissemination of the infection through the lungs. These same authors state that mild inactive pulmonary tuberculosis seems to have no effect *per se* upon the puerperium, hemorrhage is no greater, and involution is not retarded. In more active progressive cases, hemorrhage is apt to be profuse and involution delayed.

The opinion of these authors is certainly correct in the general sense, yet there are patients who have moderately advanced lesions, who are weak, short of breath, and have a rapid pulse, who go through labor with no apparent exaggeration of these symptoms. On the other hand, some who have the mildest sort of lesion and who seem strong and vigorous with no dyspnea or tachycardia will go to pieces early in labor. We should, therefore, be prepared for

immediate delivery in all cases and should conserve the patient's strength as much as possible. In many cases, morphia alone or with magnesium sulphate is sufficient. In others, rectal anelgesia is applicable. The ideal anesthetic, where it is feasible, is nitrous oxide, which may be given in sufficient amounts to control the pain and conserve the patient's energy over a period of several hours.

Many cases will do well until near the end of pregnancy, when, two or three weeks before term, they begin to show a loss of weight, a more severe cough, a more rapid pulse or perhaps a small pulmonary hemorrhage. In such cases, there should be no hesitancy in inducing labor. The rectal tube and the gauze packing mentioned earlier in this paper are very applicable for this purpose.

The after care of the mild case who has withstood the strain of pregnancy and labor is little different from that for the normal patient, except that it should be prolonged. The after care of the so-called bed patient, who was sick enough to have been in bed before delivery, should be more drastic. She should be returned to her former regime as soon as possible under the direction of a chest man.

The tuberculous mother with any activity whatsoever should never nurse the baby. The points I have tried to emphasize in this paper are:

(1) The need of medically supervised contraceptive methods for the tuberculous, especially the poor and ignorant.

(2) The importance of proper care during the first trimester of nausea and vomiting.

(3) The importance of having in consultation at all times a man especially trained in chest diseases.

(4) The value of bed rest.

(5) Many tuberculous women with proper care can be taken safely through pregnancy.

(6) Labor should be made easy and short and the attendant should be ready for immediate delivery at all times.

(7) If there is any activity in the lungs the baby should not nurse and should be separated from the mother.

(8) We should not be governed by the medical aspect alone, when economics and other factors play an important part.

(9) Each patient is a problem unto herself.

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DISCUSSION (*Abstract*)

Dr. T. B. Sellers, New Orleans, La.—My experience with pulmonary tuberculosis complicated by pregnancy has been limited, but the few cases which I have permitted to go to term have resulted very discouragingly. Recently, it has been my practice, after consultation with a capable internist, to determine the presence of a tuberculous infection, to recommend that the uterus be emptied in all cases of early pregnancy with active pulmonary tuberculosis. This is a debatable question in the quiescent cases. In cases of this type, I feel that the wishes of the woman and her husband should be of primary importance, especially in view of the fact that it is many times practically impossible to tell which cases will do well and which badly. If the woman is willing to run the risk of losing her life that the unborn child may live, or, if her religious feeling is against emptying the uterus, I abide by her wishes, even if her opinion is contrary to professional judgment. The methods of inducing labor vary with the individual case. X-ray has been advocated by some and is supposed to have a two-fold effect in that it not only induces labor, but also temporarily sterilizes the patient.

The diagnosis of early pregnancy is often a difficult task and we have found the sugar tolerance test of great value, of course coupled with a careful examination.

I agree with the majority of men that after the fifth month it is usually better to permit the pregnancy to continue until the child is viable.

Barnes and others have recently made valuable contributions to the study of the problem of tuberculosis and pregnancy, but there is still a discrepancy in statistics and a wide difference of opinion among obstetricians. This is probably due to two factors: (1) most statistics compiled are from institutions where the tuberculous patient has either already been educated prior to pregnancy or where she can receive instruction early enough to be of value in the current pregnancy; and (2) data are collected from individuals or from maternity clinics in large cities whose patients are uninstitutionalized and naturally untrained as to prophylaxis and who often live in poor hygienic surroundings. Conservatively speaking, 90 per cent of pregnant tuberculous patients cannot or will not submit to hospitalization. Therefore, we must outline a method of procedure which will be applicable not only to the small number of patients who can receive ideal treatment, but also to the great majority who cannot.

The best method of delivery must be determined by the study of the individual case and no set rules can be laid down. In primiparae with active tuberculosis, cesarean section under local anesthesia is my choice.

Spinal anesthesia has been used very effectively by some men.

Under no condition should a baby be nursed by a mother with active pulmonary involvement.

Dr. L. J. Moorman, Oklahoma City, Okla.—About 4,000 tuberculous women present themselves annually to obstetricians because of pregnancy. The obstetrician is charged with the grave responsibility of determining whether or not pregnancy shall be interrupted, and if not interrupted, what shall be the disposal of the new born baby. The question of contact is a most vital one and must have due consideration.

Dr. White (closing).—The point has been brought out that the chest men are up in the air about this problem. It is true in a measure, but there are certain definite conclusions upon which most of us agree, notably: activity of tuberculosis of any degree is an indication to terminate pregnancy during the early months. In a woman with questionable activity or a healed lesion who cannot submit to the proper regime for economic or social reasons, pregnancy should be terminated. The sanitarium trained patient is a better risk than one who has not been taught how to take care of herself and protect others.

CANCER OF THE COLON AND RECTUM: A PLEA FOR EARLY DIAGNOSIS*

By L. CARL SANDERS, M.D.,
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The mechanism by which cancer of the colon and rectum develops is not definitely known. Handley[1] brings forward some facts and observations accumulated over many years, which tend to show that chronic lymph stasis, however caused, is an important factor in determining the onset of malignant growths. He states that multiple polypi of the large intestine and hypertrophied anal papillae are the result of lymphatic congestion. These benign growths often become malignant.

Ewing[2] has observed that anatomic relations influence the development of tumors at the ileocecal valve, at the juncture of the appendix and at the rectal folds, where there are more or less definite interruptions in the structure of the intestinal wall. This is illustrated by a number of tumors occurring at these sites in children.

Bargen,[3] in a recent study of 200 cases of chronic ulcerative colitis, reported the presence of carcinoma in twenty instances. Polyposis is common in chronic ulcerative colitis and a large per cent of polypi become malignant.

McCauley[4] regards cancer of the colon as exhibiting three distinct phases:

(1) The precancerous stage.
(2) The latent stage.
(3) The stage of observable clinical symptoms.

In the precancerous stage, a lesion is present which is capable of developing and, if untreated, does develop carcinoma. He quotes Dukes as follows:

"First, the occurrence of small localized areas of epithelial hyperplasia from which arise a crop of adenomata; next, the formation of an adenocarcinoma from one of these areas or in the neighboring epithelium; finally, when the definite transition to cancer has been effected in one of these little tumors, the others tend to undergo retrogression and they are not prominent in the stage of developed cancer."

The most common type of polypus found in the colon is the adenomatous variety. The sigmoid colon is the most frequent site of polypi and 50 per cent of cancers of the large bowel occur in the sigmoid flexure.

The latent stage is that in which cancer is present, but shows no sign of its existence. This is the silent phase. It is remarkable to what extent non-obstructing cancers can grow without producing definite symptoms. It is not uncommon for the accidental discovery of a lump by the patient to be the first sign of the disease. It is in this type that the development of anemia, which is almost a constant feature of cancer of the proximal colon, is of special significance. The latent stage of cancer is not unlike that observed in syphilis. All students of syphilis have seen untreated patients who have been free of clinical symptoms many years after the primary infection.

The Stage of Observable Clinical Symptoms.—This is the beginning of ulceration or constriction, which ushers in the clinical symptoms. It is the time when the disease can be recognized clinically, often too late for successful treatment.

Incidence.—Approximately 50 per cent of all cancers occur in the gastrointestinal tract. Nothnagel's[5] series of 343 intestinal carcinomata showed 164 in the colon, 162 in the rectum, and 23 in the small bowel. Kaufmann found 64 in the colon to 51 in the rectum. The Mayo Clinic series up to 1928 included cancer of the stomach, 1,689; colon and rectum, 1,822; small intestines, 24. At The Polyclinic we have seen 20 in the colon; 23 in the rectum and rectosigmoid; 66 in the stomach, and 8 in the small bowel.

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Classification.—Ewing[2] classifies cancer of the colon and rectum into six pathological divisions. Clinically and for the purpose of discussion two main groups are observed: the large, soft, degenerating cauliflower growths in the proximal bowel and the smaller napkin ring, stenosing tumor of the distal bowel.

Pathologically, the growths in the right half of the colon present large, elevated, ulcerating surfaces, bleeding easily and lending themselves readily to infection, but they rarely produce obstruction. They seldom encircle the whole circumference of the bowel. On the other hand, the distal growths usually invade the lateral wall and encroach upon the circumference of the lumen. Obstructive symptoms are common. Acute intestinal obstruction from a malignant growth is an extremely grave condition and demands immediate attention and keen judgment in its management.

Symptoms.—If cancer of the large bowel could be recognized in the stage of development or during the latent stage, it could be eradicated in a high per cent of the cases. Unfortunately, the symptoms are so insidious that patients often have no warning until a fairly large growth is present. Unusual rumbling of gas or a feeling of fullness in the abdomen is often the first symptom.

An ulcerating growth in the bowel wall is an irritant which the bowel seeks to expel. As a consequence of its presence, new and deleterious elements are added to the intestinal contents. These are: (a) excess of mucus from the cells of the tumor and from the irritated mucous membrane, a feature which sometimes leads to an erroneous diagnosis of mucus colitis. Ochsenhirt,[6] following the classification of Broders,[12] found that the presence of mucus in carcinoma of the large intestine is the result of partial differentiation of the carcinoma. The more malignant the carcinoma, the less numerous are the secreting cells and vice versa. (b) Small quantities of blood due to traumatism and ulceration. This small amount may pass unnoticed unless the stools are examined for occult blood. Later, of course, as the ulceration increases, larger hemorrhages will present sufficient blood to be observed macroscopically. (c) Septic material from the ulcer, which in such environment cannot long remain free from secondary infection. This is particularly true of lesions in the proximal colon.

The combined result of the presence of an irritating growth and local accumulation of septic material increases functional activity. Increased peristalsis results in diarrhea, mainly of the mucous type. In growths involving the proximal loop, diarrhea is the rule, especially in elderly people. Brown[7] found diarrhea in 36 per cent of his proximal and distal groups.

A patient of ours, 84 years of age, complained of diarrhea of three months' duration. An obstructing carcinoma of the sigmoid was found which had perforated into the bowel, establishing a vesico-sigmoid fistula. The proximal bowel was impacted with feces and the diarrhea was caused by urine accumulating within the rectum.

It has long been observed that cancer of the right half of the colon produces a more severe grade of anemia than carcinoma at any other part of the bowel. Alvarez[8] studied a large number of patients with cancer in all parts of the colon and came to the conclusion that several factors were responsible for this anemia. First, the cecum has a larger diameter (6 cm.) than the sigmoid (2.5 cm.). Corresponding in the same ratio, the tumors of the cecum averaged 51.6 x 2 sq. cm. and the sigmoid tumors 31.3 x 1.75 sq. cm. The tumors of the cecum, therefore, had a much larger ulcerating surface. Second, carcinomata of the cecum are bathed in the most highly infectious fluid found in the body. This fluid, teeming with bacteria, when injected into animals causes a severe anemia to develop. Further, it was shown that when a patient with carcinoma of the cecum and a severe anemia has a short-circuiting operation, leaving the tumor but diverting the contents through another channel, the anemia rapidly clears up. Third, a number of records indicated that the factor of intestinal obstruction was also an important one. Whatever the explanation, the anemia in proximal colon cancers remains a striking clinical observation.

When the tumor at any segment of the bowel progresses to the point of obstruction, the growth delays the fecal stream, but for a time compensation is effected by the dilatation of the bowel above the lesion. As the constriction increases, peristalsis becomes more vigorous and colicky pains result. The pains are attended by the rumbling of flatus and are made worse by purgation. They often follow the taking of food. This fact is especially observed in lesions of the cecum, ascending and transverse colon. The pain is often ascribed to dyspepsia or to

gall-bladder disease, because the location is usually in the right upper abdominal quadrant. Three of our patients had been treated elsewhere for cholecystitis before the true nature of the disease was recognized.

As the obstruction progresses further dilatation of the bowel above the lesion becomes apparent and visible peristalsis occurs during the attack of pain. This is pathognomonic of obstruction.

In cancers of the left colon obstruction is the rule; in cancers of the right colon obstruction is the exception. Burgess[9] figures are 27 and 13 per cent, respectively.

Weight loss is in direct proportion to the duration and severity of the clinical course. In the presence of obstruction, the taking of food produces pain and the food is limited in quantity.

Symptoms of Carcinoma of the Rectum.—Bleeding occurs in about 90 per cent. The blood may appear as small quantities in the stool or in the form of a massive hemorrhage. Hemorrhoids are so common a source of rectal bleeding that this symptom, unfortunately, often passes unnoticed. A patient whom we recently examined and found with a large bleeding carcinoma of the upper rectum had been operated upon elsewhere two weeks previously for hemorrhoids. It is a good plan to make a proctoscopic examination on every patient with symptoms of fresh bleeding from the rectum, regardless of the presence of hemorrhoids which may appear to be the source of the bleeding.

Practically all of the tumors arising within the rectum are the stenosing or napkin ring type and obstruction with delay in the fecal column follows. Soon diarrhea appears, alternating with constipation. The diarrhea is more of a tenesmus with the passage of small quantities of bloody mucus, often unmixed with fecal matter.

Pain is rare in the early lesions. It appears when obstruction begins and is the one symptom which arouses suspicion and fear in the mind of the patient. At first there is a sense of pressure and fullness in the rectum. As the bowel attempts to expel the irritating mass, the pain becomes colicky, is referred to the bladder, the sacrum or perineum.

In arriving at the correct diagnosis of malignancies of the colon and rectum, a definite plan of procedure is necessary.

(1) A careful history, with particular attention to the character of the onset, the persistence of a definite change in the bowel habit, from regular to irregular; the presence of blood in the stool, whether fresh or cold; pain, its location, time of onset in relation to the taking of food; flatulence and distension with rumbling of gas; unexplained anemia; vague abdominal discomfort and dyspepsia. It must be remembered that loss of weight and cachexia occur only in advanced cases.

(2) Physical examination will show anemia, local distension, visible peristalsis or the presence of a palpable tumor. A digital examination of the rectum is best made with the patient lying on the left side with the knees flexed on the abdomen.

(3) The proctoscope is as valuable an instrument as the cystoscope and should be more generally used. Very early lesions of the rectosigmoid are easily visualized. Since cancer of the rectum and sigmoid metastasize early, it is important to recognize lesions in this segment as soon as possible.

(4) The feces should be examined for blood, mucus, and fragments of degenerating tissue. Persistent occult blood in the stool indicates ulceration above the rectum.

(5) *Roentgenologic Examination.*—For a satisfactory study of the colon, proper cleansing of the bowel is necessary. The presence of gas bubbles and fecal matter may obscure the pathology. Visualization of the colon during the administration of the barium is very necessary. The plain roentgenogram alone is often confusing.

The characteristic roentgen finding is a constant filling defect. Frequently a mass can be palpated during the examination. Inflammatory lesions may also cause filling defects, but these are not so constant, especially if a reexamination is made following the administration of belladonna to physiologic effect. Occasionally the only roentgen finding is obstruction.

Differential Diagnosis.—There are certain diagnostic difficulties which may arise in the course of an examination. It is often difficult to distinguish between diverticulitis and carcinoma. Here the symptoms of inflammation, the local tenderness and the presence of other diverticula are helpful. Malignancy may follow diverticulitis.

Chronic ulcerative colitis shows the rigid bowel with narrowed lumen and according to

Buie[10] can be diagnosed through the proctoscope. It is to be recalled that Bargen[3] found 10 per cent of his chronic ulcerative colitis cases with malignant polyposis.

A tumor in the proximal colon is to be differentiated from tuberculosis of the cecum, chronic appendiceal abscess, mucoid appendix and actinomycosis. Appendiceal abscess only follows an acute attack of appendicitis and may be diagnosed by the history and blood findings. Actinomycosis is uncommon, is accompanied by fever and the mass often perforates, forming a sinus through the abdominal wall.

Several years ago we saw a patient with a tumor in the right abdomen the size of a normal kidney, which had been present for ten years. There was a smooth filling defect in the cecum. Pyelography demonstrated the right kidney above the tumor. At operation an enormous cystoid appendix was removed.

Even with a careful history and the best of technic in making examinations, errors in diagnosis occur. However, if investigation of obscure abdominal symptoms is carried out, more cases of operable carcinoma of the bowel will be found.

To emphasize the importance of early diagnosis, a review of 43 of our cases of carcinoma of the colon and rectum is given.

The usual ratio of males to females is two to one. In our series the percentage is about equal.

It is becoming more generally recognized that cancer of the lower bowel may occur in early life. There are 53 cases in the literature of carcinoma of the rectum in patients under twenty years of age.

Cancer involves the colon about as frequently as it does the rectum. *Chart I* reveals 23 cases in the rectum and rectosigmoid to 20 in the colon.

A glance at *Chart II* shows that the first symptom to appear was abdominal pain in 20; bleeding from the bowel in 10; constipation in 5; diarrhea in 3. When a patient in the cancer age complains of intermittent abdominal pain, passes blood in the stool or has a sudden change in his bowel habit, it is an indication for a careful study of the gastrointestinal tract.

Chart I

Sex		Age		Location of Tumors	
Males	21	Youngest	28	Transverse colon	8
Females	22	Oldest	84	Cecum and ascending colon	8
	—		—	Sigmoid	4
Total	43	Average	56	Rectum and rectosigmoid	23

Chart II

First Symptoms to Appear		Analysis of Symptoms and Findings	
Abdominal pain	20	Bleeding from the bowel	22
Bleeding from bowel	10	Abdominal or rectal pain	35
Constipation	5	Constipation	25
Diarrhea	3	Diarrhea	19
Palpable tumor	1	Palpable tumor	31
Hemorrhoids	1	Nausea and vomiting	11
Dysuria	1	Tumor perforated	10
Loss of weight	1	Obstruction	26
Flatulence	1	Abdominal swelling and gas	20
Total	43	Average duration of symptoms 1 year.	

All of the rectal and rectosigmoid tumors were seen through the proctoscope. Eight of the colon tumors, including four in the transverse colon, three in the cecum and one in the sigmoid were palpitated at the original examination. At operation 10 had perforated and 26 were obstructing the bowel lumen.

Twenty-nine patients were operated upon. The tumor was resected in 18; palliative colostomy was done on 3 to relieve obstruction; 8 had extensive metastasis and were closed without an attempt at resection; the disease had advanced so far in 8 that exploration was not advisable; 6 refused operation.

Nine patients died within two weeks after operation. They were all in poor physical condition and succumbed to postoperative shock. Ten died with general carcinomatosis within one year after operation; 12 of the patients who were not operated upon are dead; one is living after two years. This patient had a constricting growth at the internal rectal sphincter which

Chart III

Treatment			
Total operated upon	29	Living after resection 1 to 8 years	10
Tumor resected	18	Death postoperative	9
Colostomy only (inop.)	3	Dead within 1 year	10
Exploration only (inop.)	8	Deaths unoperated upon	12
Inoperable, no exploration	8	Living unoperated upon	1
Operation refused	6	Not traced	1

clinically appeared to be carcinoma. Biopsy was not done, so the diagnosis may have been in error. One patient we have failed to trace.

Ten patients are living from one to eight years after resection of the tumor. The high death rate in this series can be explained by a study of the accompanying charts. It will be seen that the average duration of symptoms was one year. Twenty-six patients had obstructive lesions; 31 had palpable tumors and 35 complained of abdominal cramps. This means that the disease had advanced to the stage of ulceration and obstruction at the time of examination. Further, there were 25 with demonstrable metastasis.

From the results obtained in the 18 cases where the tumors were resected, it will be observed that 9 had advanced so far that the operative mortality was beyond the normal expectancy.

Rankin[11] reported a series of 122 patients operated upon for colloid carcinoma of the rectum and colon. Twenty-three died from the operation; of the remaining 99, 22 were traced. Sixty were dead and 32 were living.

A review of the literature reveals few contributions on cancer of the colon and rectum by medical men. The profession is indebted to the surgeon for the majority of the facts pertaining to malignancies of the gastrointestinal tract. One may well ask, why have the internist and the general practitioner refrained from writing more on cancer of the bowel? True, cancer is a surgical disease, but the diagnosis is strictly a medical problem. If we as medical men studied the end results in the surgical treatment of cancer of the colon and rectum, we could not help but feel lax in our duty in not diagnosing and referring to the surgeon more cases favorable for cure.

SUMMARY

(1) Lymphatic stasis seems to be a plausible theory of the development of cancer of the lower bowel.

(2) Three stages of development are considered: (1) the precancerous stage; (2) the latent period; and (3) the stage of observable clinical symptoms.

(3) The onset is insidious. Symptoms vary according to the location of the tumor. Abdominal pain, bloody stools, loss of weight and cachexia are late symptoms.

(4) For making an early diagnosis, a careful history, a physical examination, proctoscopic examination, a study of the warm feces and a roentgenogram of the colon are necessary.

(5) Forty-three cases with an analysis of the symptoms, findings and operative results are reviewed.

(6) The responsibility for making an early diagnosis rests upon the physician. If investigations of the colon and rectum are made in patients presenting vague abdominal symptoms, more cases of early cancer of the bowel will be found and cured.

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DISCUSSION (*Abstract*)

Dr. J. H. Musser, New Orleans, La.—Dr. Sanders called attention to the infrequency with which this condition is diagnosed in time to be of any avail to the patient. One patient out of every three did not survive operation. We should impress upon the general practitioner that carcinoma of the intestinal tract frequently goes undiagnosed over a long period of time. The average practitioner does not often see these cases. Even in clinics with a large number of patients such as the Mayo Clinic, or Dr. Sanders' clinic, relatively few cases of this particular type of cancer are seen. The general practitioner naturally thinks of the conditions that are more frequent.

I am particularly interested in the anemia that occurs in connection with carcinoma of the intestinal tract. These anemias develop with remarkable rapidity, with such speed often that the anemia clouds the clinical picture. Incidentally, the anemia frequently develops rapidly when the local lesion is still amenable to operative treatment. Dr. Sanders reports that this anemia is a constant accompaniment of carcinoma of the colon.

Some years ago Dr. Cabot said that the onset of indigestion in an individual past forty-five is always suggestive of carcinoma of the stomach. The same

thing might be said of intestinal indigestion. When a patient beyond the age of fifty develops symptoms of intestinal indigestion we should suspect carcinoma. Bear in mind, however, that although this type of malignancy does occur in relatively young people, they are the exceptions.

One of the other features that we should instruct the general practitioner in is in the use of the proctoscope. Of course, you gentlemen are specialists in your field and you use a proctoscope just as I use a stethoscope, but if the average practitioner could be taught to use the proctoscope as frequently as he uses a tongue depressor, he could recognize malignancies of the lower bowel or rectum or sigmoid much more frequently than he does now.

The first symptom that Dr. Sanders called attention to in his table was pain. Of course that is the symptom which naturally is most likely to bring the patient to the physician. Nevertheless, I do not think we realize quite as we should the importance of the symptom of pain in gastrointestinal malignancy. Some years ago in analyzing a series of cases of carcinoma of the stomach I found that 43 per cent of the patients came to the physician because of pain. I think that symptom should be emphasized.

Dr. Julius Friedenwald, Baltimore, Md.—In a series of 64 cases of cancer of the colon and rectum studied by Rosenthal and myself in 1925, there were 32 of the rectum, 20 of the sigmoid, 2 of the cecum and ascending colon, 4 of the hepatic flexure, 1 of the transverse colon, 4 of the splenic flexure and 1 of the ascending colon.

In evaluating the significance of the various signs and symptoms of cancer of the colon, it is quite evident, as Dr. Sanders has shown, that many are general manifestations frequently present in other intestinal affections and not characteristic of this condition alone. The more characteristic developments are usually late developments. On this account the late diagnosis of cancer is rendered exceedingly simple, while the early diagnosis is usually difficult. In most instances, however, of early cancer of the bowel, there are so few manifestations that the diagnosis may be impossible, while in others the early recognition may be masked by the presence of atypical symptoms. Evidence of stenosis of the bowel, usually the first alarming manifestation, occurs late in the course of the disease and increasing constipation may not appear until a fairly marked degree of obstruction has been produced. It is extremely important, however, to view with suspicion all patients over 35 years of age who present a progressively increasing constipation associated with the passage of blood in the stools, even though this be but of the occult type. In all such instances routine proctoscopic examinations should be made as well as thorough and repeated x-ray studies. The latter not infrequently supply us with direct evidence of the presence of growths, where other signs still remain inconclusive. It is, therefore, only by means of most careful investigations into the signs and symptoms together with painstaking examinations, that we can hope for an early recognition of cancer of the colon at that period when a radical cure may still be expected from surgical intervention. For it is a well recognized fact that certain colonic tumors, due to their location as well as slowness in their growth, are far more favorable for radical surgical procedures than others higher up in the digestive tract.

Dr. Sanders (closing).—The history is a very important factor as a lead to the diagnosis. One of the first symptoms, in some cases, is the rumbling of gas in the intestines. Another is constipation. When a patient in middle life complains of these two symptoms coming on after previously normal habits of elimination, it is an indication for a careful examination of the gastrointestinal tract.

BLOOD TRANSFUSION*

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HISTORICAL

Blood transfusion as we see it is not a recent innovation. In fact, it was attempted by the ancients, and in 1492 Pope Innocent VIII was supposed to have been transfused by a Jewish doctor. The three young boys who furnished the blood all died and the Pope received no benefit. The blood was probably given by mouth, as the circulation of blood was not discovered by Harvey until one hundred and fifteen years later.

About twenty-five years ago Crile re-introduced blood transfusions as a method of treatment. He actually joined the artery of the donor to the vein of the recipient. Since then various methods have been used to do transfusions and the advances in our knowledge and mode of transfusions are attributable to the work of Moss, Linderman, Bernheim, Lewisohn, Kimpton and Brown and others. There are two methods in use at the present time, namely, the transfusion or infusion of citrated blood and the use of whole blood. The transfusion of whole blood may be accomplished by the use of the Kimpton-Brown tube and its modification, the Vincent tube, and certain apparatus such as the Unger, Soresi and Scannell.

INDICATIONS

We believe that there are certain definite indications for the use of blood transfusions. Such indications may be listed as follows:

(1) *Massive Hemorrhage.*—In such a case the introduction of blood not only fills up the vessels with fluid, but also furnishes red blood

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cells, which of course have the capacity of carrying oxygen, a most important factor. In cases of massive hemorrhage we believe the citrate method is most useful on account of its simplicity of technic and the rapidity with which it can be done.

(2) *Anemias.*—In the anemias due to small continuous bleeding, transfusion has a place. It introduces blood platelets and fibrinogen, and has the stimulating effect of new blood. In this respect it is much more valuable than the introduction of serum for the same purpose.

(3) *A Preoperative and Postoperative Measure.*—We see frequently various types of cases that badly need surgery, and often the patient is in no condition to withstand the operation. Such individuals, by the use of blood transfusion, one or several, can easily be brought to the point where surgery may be safely attempted.

We are greatly surprised in reading the literature on this subject to find the large amount of blood loss which takes place in two or three types of operations. This question was carefully studied by Ward, who found that in radical operation for mammary carcinoma the blood loss was about 700 c. c. In nephrectomy it was about 800 c. c.; in radical hysterectomy, 250 c. c.; in ordinary perineal and cervical repair, 300 c. c. In a patient who is not in good physical condition, knowing there will be the added burden of loss of blood, it is an exceedingly wise procedure to resort to transfusion before operation. It is much better to have the entire campaign formulated and to be ready for an emergency than to have an emergency arise and then have to hunt about for a suitable donor to give the blood.

(4) *Sepsis.*—In the treatment of septicemia we believe blood transfusion is of much more value than the introduction of mercurochrome, gentian violet, metaphen or any of the other bactericidal substances. When transfusion is done, we introduce fresh phagocytes, fresh bactericidal substances, fresh complement, fresh vitality, and these factors assist the patient in overcoming the infection. Some authorities advise against transfusion in various acute infections. To our mind it certainly cannot do any harm and may do a great deal of good.

We had under observation some months ago a case of puerperal infection and pelvic thrombophlebitis in a young woman. Her temperature was 103 to 104° F. and she had emboli in various parts of her body and skin. She was transfused, following which for two or three days her temperature remained high, then gradually receded and she made a complete recovery. It is true she might have gone through this without transfusion, but she had made no progress for five weeks, and as the blood count was increased by the procedure and continued so, most of the introduced blood remained in the body.

In cases of sepsis the introduction of blood is advisable because of its bactericidal and phagocytic properties; it also assists in raising the patient's resistance. Such transfusions should be of whole blood unmodified. Citrated blood is not so satisfactory.

(5) *Blood Dyscrasias.*—Although blood transfusion has never cured a case of pernicious anemia, the introduction of blood will carry these patients over the crisis until they reach the stage of amelioration, after which they may go along for several years in a very comfortable way.

BLOOD GROUPING

The selection of a suitable donor is the most important preoperative safeguard of transfusion. As a rule men are preferred to women. The latter are more apt to be anemic; their veins are harder to find and they recover from loss of blood more slowly than men. The donor should be in good health, especially free of asthma and the less easily recognized malaria and syphilis. A recent Wassermann or Kahn test should be insisted on. A hemoglobin test and red cell count should be made since professional donors and relatives offering themselves sometimes give lower readings than the patients. As a final safeguard in the selection of a donor his blood should be cross-matched with that of the patient, the cells of each being tested against the serum of the other. We consider this necessary to avoid the possible errors of typing and to avoid atypical groups. In our experience, we have met with donors incorrectly typed, the donor usually being placed erroneously in Group 4 (Moss). This error has resulted from (1) too short a period of observation of the typing set up; (2) use of old serum of decreased potency; (3) or a combination of both of these factors. A minimum of thirty minutes should be adopted for emergency transfusions; for patients in a cachectic state of long duration, a minimum of one hour's observation of the typing and matching should be adopted. Another source of error is the occurrence of incompatibility between people who according to routine blood typing fall into the same group. We have in mind one patient in Group 2 whose serum regularly agglutinated the corpuscles of several donors in the same group after twenty minutes, and agglutinated also the corpuscles of a universal

donor. The patient's and donor's blood in this case were rechecked carefully several times. The universal donor tried had been typed several times previously in different hospitals and used a number of times as a Group 4 (Moss) without bad results. In the above case his corpuscles were agglutinated by the patient's serum after twenty minutes. Physicians differ regarding the use of universal donors for patients belonging to other groups, some declining to use them because of the danger of causing agglutination of the patient's red corpuscles. Since the serum of a Group 4 (Moss) may have unusual agglutinating power, the amount of blood given in such cases should be less than that normally given. It should be used only after the donor's corpuscles have been matched against the patient's serum.

VINCENT TUBE METHOD

In our own work we employ by preference the Vincent tube to do transfusions. This tube is a modification of the Kimpton-Brown in that the stem is ground to fit a needle which may be introduced into the vein of the donor. When the tube is full it is disconnected from the needle and attached to a similar needle in the vein of the recipient, or if the open method is used the stem can be inserted directly into the vein of the recipient.

The great objection to the use of the Kimpton-Brown or the Vincent tube was the trouble and difficulty in getting a smooth layer of paraffin in the tube. Formerly either the nurse or the physician would heat the tube in which the paraffin was placed and allow the melted paraffin to coat the inside of the tube by gradually rotating the tube. The paraffin layer was thick in places and in other areas there would be no paraffin and the procedure was a burden. But now the method of paraffining the tube is relatively simple. A sterile solution of paraffin and ether is poured into the tube, the tube is turned and the excess fluid poured out. Immediately there is a fine even layer of paraffin over the inside of the tube.

This solution is made up of ordinary paraffin sterilized in the autoclave for three successive days and while still warm dissolved in ether.

CITRATE METHOD

The presentation of the citrate method of transfusion is not done with the intention of advocating it in preference to one of the whole blood methods. The latter are more rational physiologically and are particularly indicated in cases of chronic sepsis with anemia and in cases resulting from a disturbance of the blood-forming organs.

The citrate method has in its favor simplicity of technic and equipment and fortunately is most efficacious in those emergency hemorrhage cases which occur where hospital facilities and trained specialists are not readily available. Any one who can give intravenous medication can give a citrate transfusion. Matching of the donor and recipient by cross-agglutination tests is, of course, preferable and should be done whenever possible, but where urgency demands it the use of a universal donor is permissible, although the reaction may be more severe.

In the rather isolated communities it would be well to have some healthy young man typed and a list kept of those belonging to Group 4 and of the Moss classification, which embraces the so-called universal donors. Such men could be called upon when needed.

The necessary equipment consists of:

Skin antiseptic (iodine).
Some sterile towels, gloves, and gauze.
A tourniquet.
Two needles of 16 gauge diameter (or larger).
A graduated beaker (500 c. c.).
A glass stirring rod.
One 50 c. c. ampoule of 2.5 per cent sodium citrate solution.
An ordinary infusion flask and connecting tubing.
Scalpel, scissors, forceps, needles, cat-gut, novocaine, and syringe if veins are not accessible.

The technic is as follows:

Sterilize and inspect all equipment.
Prepare skin overlying accessible veins of both donor and recipient and drape with sterile towels.
Place entire contents of one 50 c. c. ampoule of sodium citrate solution into a graduated beaker.
Apply tourniquet to donor.
Insert needle into his vein and allow blood to fill beaker to 500 c. c. mark, stirring the citrate and blood mixture slowly and continuously with the glass rod.
Release donor's tourniquet and withdraw the needle.
Transfer blood to infusion flask, filtering it through one or two layers of gauze.
Apply tourniquet to recipient.
Insert needle into suitable vein.
Release recipient's tourniquet.
Connect flask tubing to needle after expelling air and let the blood flow in by gravity pressure, giving all in the usual adult case unless chill, headache, cough, dyspnea or marked cardiac palpitation appear.
Withdraw the needle and keep patient quiet, giving later symptomatic treatment if occasion arises.

REACTIONS

In the past ten years the performance of blood transfusion has ceased to be a rare and spectac-

ular procedure and is now a common and widespread mode of treatment of a great variety of conditions. The newer methods to accomplish blood transfusions have made it a very simple procedure. However, the taking of blood from one patient and putting it into another is not without a certain amount of danger. Reactions may occur as a result of infusion of blood into a patient which may be most serious.

These were investigated by Kordenat and Smithies, who in a very comprehensive article did not attempt to compare the results of different men nor the different methods, but studied the reactions following the introduction of whole blood by the use of the Kimpton tube. It was found that they might take one of two forms: first, the hemolytic form which developed immediately upon the introduction of a limited amount of blood. We have seen two such cases. One patient recovered and the other died.

In the first case a man with pernicious anemia began vomiting almost immediately after the introduction of blood was started and transfusion was stopped. In half an hour he was icteric, had hemoglobinuria, hematemesis and passed blood by rectum. He finally recovered and his anemia was improved. The other case was similar, but although the anemia was apparently not so severe, the man died following transfusion.

Another type of reaction develops more slowly and is a form of anaphylactic reaction. In the fulminating or hemolytic type there is diminution of platelets, a reduction in erythrocytes with a decrease in polymorphonuclears, and an increase in the lymphocytes. The bleeding time is increased and the coagulation time is lengthened. In the second type, no hemolysis takes place; the erythrocyte count remains unchanged, the polymorphonuclears are not diminished, and the coagulation time is shortened, showing that apparently no hemolysis occurs. This reaction appears generally four or five hours following transfusion. It is characterized by a chill and a temperature of 104 to 105° F. The pulse is correspondingly elevated, but there is no change in respirations. The temperature recedes by lysis and usually in two days is normal and the effect of the transfusion is not lost. This is the type seen in infections where transfusions are performed. It is explained by some to be due to the action of bacteria breaking up the blood cells in the serum, or to the new blood disintegrating the bacteria and so liberating protein, the so-called protein reaction, which appears when the phagocytes and bactericidal substances that have been introduced overcome the infection. The only danger in a reaction of this type is in cases where there is a damaged heart, kidney or liver. In some cases death has followed due to renal complications.

CONCLUSIONS

In conclusion, we would say that blood transfusion is:

(1) A preoperative and postoperative measure of inestimable value.

(2) In the treatment of infections, the introduction of whole blood not only increases the vitality of the patient, but helps him overcome his infection.

(3) In anemias, blood transfusion, while not a curative agent, offers the patient a boost and may carry him past a crisis.

(4) Reactions can be avoided by careful grouping and especially by cross-matching.

(5) The introduction of whole blood is better than citrated blood wherever transfusion is indicated, except possibly in acute hemorrhage.

SKIN LESIONS ENCOUNTERED AMONG ALLERGIC INDIVIDUALS*

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The purpose of this paper is to call attention again to the frequency with which certain dermatoses are associated with hay-fever, asthma and other allergic phenomena. A careful study of these conditions, together with their hereditary characteristics, strongly suggests that, in many instances at least, they are essentially the same in nature, differing only in the kind and location of the cells involved. The following is an illustrative case:

A woman, 55 years of age, has had hay-fever for 25 years. The symptoms occur during the fall months only and have been proved to be due to wind-borne pollens. Contact with pyrethrum invariably produces an attack of asthma regardless of the time of year, and the ingestion of honey or celery will just as surely cause violent urticaria.

This study is based on an analysis of the records of 800 individuals regarded as possibly allergic because of the nature of their symptoms or past histories. At times it was difficult to select the chief complaint, as the following case exemplifies:

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A child, three and one-half years of age, developed eczema when five weeks old. At the age of ten months the mother noticed that when peas and eggs were added to the diet vomiting immediately occurred. At eighteen months urticaria appeared. Skin tests at this time gave strongly positive reactions to a number of foods, the elimination of which promptly relieved the skin trouble. Later, she developed hay-fever and asthma, but is free from all these conditions at present. Eczema or urticaria can be induced at will, however, by the ingestion of any of the foods to which she is known to be sensitive.

"Eczema" or "nettle-rash" was the chief complaint in 128 (16 per cent) of this series (*Table 1*), while a total of 239 (29.8 per cent) presented some type of skin lesion at the time of examination (*Table 2*). In addition, 165 (20.6 per cent) gave a history of either urticaria or eczema. Thus, one-half of the entire series presented either a dermatosis at the time of examination or gave a history of one. In this paper no close distinction has been made between the terms "eczema" and "eczematoid dermatitis" for the reason that we are dealing primarily with incidence and etiology rather than pathology.

For comparison, the records of 800 other patients were reviewed for the incidence of skin lesions at the time of the first examination. We selected at random 100 cases of each of the following diseases: pulmonary tuberculosis, chronic infectious arthritis, chronic cholecystitis, malaria, exophthalmic goiter, fibroma of the uterus, arterial hypertension, and diabetes mellitus. Skin lesions were noted in only 15, or 1.87 per cent. Of course, only those lesions which are regarded as of clinical or statistical importance were indexed. These findings were then compared with a similar series taken from the records of the Memphis General Hospital, which has a very comprehensive cross index system. Here we found the incidence less than in our private records. While observers may differ as to the incidence of these skin conditions and their relation to allergic phenomena, we believe the figures quoted above justify the assertion that allergy is a more important etiologic factor in dermatological diseases than is generally recognized.

Table 1
REVIEW OF 800 RECORDS

Chief Complaint	No. Patients	Per Cent
Hay-fever	292	36.5
Asthma	211	26.3
Eczema	43	5.3
Urticaria	85	10.6
Abdominal allergy	64	8.0
Miscellaneous	105	13.1

Table 2
FREQUENT ASSOCIATION OF SKIN LESIONS AMONG ALLERGIC INDIVIDUALS

	Number	Per Cent
Patients examined	800	100
Skin lesions present at time of examination, given as chief complaint	128 (16%)	
Skin lesions present at time of examination, but not given as chief complaint	111 (13.8%)	50.4
History of urticaria or eczema in past but no symptoms at time of examination	165 (20.6%)	

Urticaria or eczema occurred in 212 patients with hay-fever or asthma—42.1 per cent.

There has been much controversy over the use of such terms as allergy, anaphylaxis, idiosyncrasy, protein sensitization, hypersensitiveness, atopy, and the like. For the sake of simplicity and to avoid further confusion, Kolmer[1] suggests that we adopt the term "allergy" and discard all others. This we can do for clinical purposes and still appreciate the fact that, from a purely scientific viewpoint, there are certain fundamental differences between anaphylaxis in the guinea pig and an acquired sensitivity or allergy in the human. The term "allergy" as used in this discussion may be defined briefly as a "condition of altered reactivity of body cells" or it may be dressed up a bit, according to Bloch's[2] definition.

Those of us who specialize in the treatment of hay-fever and asthma have found the following conception of allergy most helpful: (a) hay-fever, asthma, certain dermatoses, and certain affections of the mucous membranes of the gastrointestinal tract are similar in nature, differing only in the kind of cells involved; (b) the symptoms are the result of an altered reactivity of these cells; (c) this altered reactivity is due to a sensitization of these cells to substances which are innocuous to normal individuals; (d) this ability to become sensitive is, in most instances, an hereditary characteristic, although the actual sensitivity is acquired.

The fact that some individuals exhibit symptoms upon the first ingestion of, or contact with, a certain substance need not confuse us if we accept the theory proposed by Shannon[3] that sensitivity may be acquired from minute amounts of protein obtained through breast milk, or the one suggested by Balyeat,[4] Ratner[5] and others that it may be acquired *in utero*.

Every one interested in scientific medicine prefers facts to theories, but when the former cannot be definitely established, theories are better than nothing if they aid in the relief of suffering. It is not contended, by any means,

that all urticaria and eczema are allergic. Far be it! One of the objects of this paper, however, is to call attention to the fact that the etiology of certain dermatoses is overlooked at times because allergy is not considered or, if suspected, is not excluded by proper means. The following case report will illustrate this point:

Miss M. N., aged 20, was referred to us in September, 1929, on account of a severe "eczema" which she had had since infancy. Incidentally, she had hay-fever, asthma and sporadic attacks of urticaria. There was a family history of eczema on the paternal side. She had consulted many physicians because of the skin condition, but without relief, and in 1927 was shown before this Section of the Southern Medical Association. On skin testing she was found to be sensitive to a variety of pollens, animal epithelials, foods and miscellaneous substances. Among the latter was silk, to which she was especially sensitive. At the present time she is free from eczema as well as hay-fever and asthma. Interestingly, it has been found that only certain types of silk will produce symptoms. Recently a "run" developed in a stocking she was wearing and shortly after mending it she noticed intense itching of the leg. On removing the stocking she found a line of irritation corresponding exactly to contact with the silk thread employed. This is in agreement with the case reported by Klauder,[6] which was due to black silk only.

The use of such expressions as "allergic rhinitis" and "allergic dermatitis" or "allergic eczema" is sometimes condemned on the ground that they tell us nothing as to etiology. Obviously no skin condition should be labeled "allergic dermatitis" until it has been proved to be allergic in origin. But what name shall we give to a skin condition that disappears when eggs, peas and lamb are eliminated from the diet and reappears when these foods are ingested again? Or to one that clears up when a dog is removed from the environment? Or one that is relieved when silk is eliminated from the apparel?

The question may then be asked, "When should allergy be suspected?" Since an etiologic differentiation between certain dermatoses cannot be made clinically, it should be considered in all cases wherein a positive family history of allergy is given, particularly if the patient has failed to obtain relief from the usual methods of treatment. Numerous writers have called attention to the importance of heredity in these conditions. In the reported statistics the incidence of heredity varies considerably, depending upon whether they are obtained from private or dispensary records. This report deals with private patients only. A recent survey of 112 children below the age of 17 and with all forms of allergy showed a positive family history in 91.06 per cent.

Tables 4 to *9* have been arranged according to age. In *Table 4* it will be seen that 21 children with eczema or urticaria, whose ages varied from 2 months to 10 years, gave a positive family history for allergy in a higher percentage than in any other group. Undoubtedly, this is ex-

Table 3
POSITIVE HISTORY OF ALLERGY

Total Number	Chief Complaint	Ancestors	Brothers Sisters	(A)	Per Cent (B and S)	Total
292	Hay-fever	179	31	61.3	10.6	71.9
211	Asthma	146	20	69.1	9.4	78.5
43	Eczema	21	3	48.8	6.9	55.7
83	Urticaria	47	4	55.2	4.7	59.9
64	Abdominal allergy	32	5	50.0	7.8	57.8
105	Miscellaneous	45	10	42.8	9.5	52.3

Note.—The miscellaneous group is composed of individuals with complaints such as indigestion, headache or various cutaneous manifestations.

Table 4
A STUDY OF THE FAMILY HISTORIES OF 128 PATIENTS WITH URTICARIA OR ECZEMA AS THE CHIEF COMPLAINT

Urticaria	Eczema	Age	Maternal	Paternal	Other Members
	+	2 mos.	Hay-fever	0	Brother—Eczema
	+	3 mos.	0	Hay-fever	0
	+	5 mos.	0	Hay-fever	0
	+	5 mos.	0	0	0
	+	7 mos.	Family history unknown		
	+	1 year	Hay-fever Eczema	Migraine	Sister—Eczema
	+	1 year	0	Eczema	0
	+	1¼	Urticaria	0	Brother—Eczema Uncle—Urticaria
	+	1½	0	Asthma Hay-fever	0
	+	1½	0	Hay-fever	0
	+	1½	Family history unknown		
+		2½	0	Asthma	0
+		2¾	Family history unknown		
+		5	Urticaria Hay-fever	0	0
+		5	Family history unk. (orp.)		
	+	5	Eczema	Asthma	Sister—Eczema
	+	7	Migraine Asthma	0	0
+		7	Hay-fever Eczema	Migraine	Sister—Eczema
+		7½	0	Asthma	0
+		8	Urticaria Migraine	Urticaria	0
+		10	Migraine	0	0

plained in part by the fact that the family history is better known among young children. Among those who gave urticaria or eczema as the chief complaint, the ages varied from 2 months to 74 years, with an average of 29.3 years.

Patients who have been tested for other diseases of the skin are listed among the miscellaneous group. Two patients with psoriasis, for example, were tested because of a positive family history for allergy. Both had had urticaria before the onset of psoriasis. The positive reactions were thought to be related to the former, but, strange to say, both report their skin lesions greatly improved after eliminating those foods which gave positive reactions. This is not an attempt, however, to place psoriasis among the allergic dermatoses.

Regarding the various methods of skin testing, their value and interpretation, there is a wide divergence of opinion. It seems unnecessary to mention that some patients, although clinically sensitive, do not always give positive skin tests and that unless the limitations of skin testing are thoroughly understood, confusion will continue. In those conditions where we might reasonably expect positive reactions, many failures have resulted in the past due to (a) faulty technic; (b) incomplete testing; (c) failure to make twenty-four-hour readings; (d) the use of poorly prepared testing materials, and (e) the exclusive employment of the scratch test. During the past ten years other methods, such as the contact, intradermal and passive transfer, have come into general use and each, when properly selected, has added considerably to this phase of the work. Positive skin tests may represent past, present or future history. They mean nothing, therefore, unless properly

Table 5

A STUDY OF THE FAMILY HISTORIES OF 128 PATIENTS WITH URTICARIA OR ECZEMA AS THE CHIEF COMPLAINT

Urticaria	Eczema	Age	Maternal	Paternal	Other Members
+		12	Hay-fever	0	0
	+	13	0	Asthma	0
+		13	Urticaria	0	0
+		14	Hay-fever	0	0
	+	15	Fam. hist. unk.		
+		16	Eczema	0	0
	+	16	Eczema Urticaria	0	0
+		16	Hay-fever	0	0
+		16	Migrane Urticaria	0	0
+		18	0	0	0
+		19	0	0	0
	+	20	0	Eczema	0
+		21	0	0	0
+		22	0	0	Sister—Urticaria
	+	22	Fam. hist. unk.		
	+	22	0	0	0
+		22	0	0	0
+		22	Eczema	Hay-fever	Sister—Asthma
	+	22	Eczema	0	Brother—Hay-fever
+		23	0	0	0
	+	23	0	0	0
+		23	Urticaria	0	Brother—Urticaria
+		23	0	0	0
+		24	0	Asthma	0
	+	24	0	0	0

Table 6

A STUDY OF THE FAMILY HISTORIES OF 128 PATIENTS WITH URTICARIA OR ECZEMA AS THE CHIEF COMPLAINT

Urticaria	Eczema	Age	Maternal	Paternal	Other Members
+		24	0	Asthma	Brother—Hay-fever
+		24	0		0
+		26	Hay-fever	0	0
+		26	0	0	0
+		26	0	Urticaria	0
+		27	0	0	0
+		27	Urticaria	0	Brother—Urticaria Sister—Urticaria
+		27	0	0	Sister—Asthma
+		27	0	Urticaria	0
	+	28	0	0	Sister—Pruritis Brother—Hay-fever Brother—Hay-fever
+		28	Fam. hist. unk.		
+		28	Asthma	0	0
+		29	0	0	0
+		29	Urticaria	0	0
+		29	Urticaria	Urticaria	0
	+	29	0	Eczema	0
	+	29	Asthma	0	Sister—Asthma
+		30	Fam. hist. unk.		
+		30	Hay-fever	Hay-fever	0
+		30	Urticaria	0	0
+		30	0	0	Sister—Hay-fever
+		30	0	Urticaria	Sister—Urticaria
+		30	0	Hay-fever	Brother—Hay-fever Child—Eczema Asthma
	+	30	0	0	0

correlated with clinical data in such a manner as to prove them etiologic factors.

To demonstrate the value of combining methods and of making twenty-four-hour readings, the following case is cited:

A child, two and one-half years of age, was brought to us on June 3, 1928, on account of attacks of edema, erythema, intense heat and profuse perspiration. The affected area was confined to the dorsum of the left hand and wrist. Attacks had occurred daily for about one year. A paternal uncle had asthma. On skin testing with all the foods comprising her diet, no reactions were obtained by the scratch method. These tests were followed by intradermal tests which were negative on immediate reading. She returned twenty-four hours later for observation and all scratch tests were again negative, but about the site where milk had been injected there was edema and erythema measuring 25 millimeters. After removal of milk from her diet the attacks promptly ceased. Later, deliberate feeding of milk produced attacks.

Vaughan[7] [8] has called attention to the value of immediate, six-hour, and twenty-four-hour readings; also to the fact that failures often result after a specific cause has been detected due to the unwise use of the information obtained. For example, we often find patients sensitive not only to one food, but to one or more foods in the same botanical family, such as wheat, rye, oat, corn and rice. Incomplete elimination of these foods often causes poor results. Other patients, who are sensitive to such things as animal hair and miscellaneous products, may fail to obtain relief because they unknowingly come in contact with these substances in various ways.

By employing both the scratch and intradermal methods and testing with foods, animal epithelias, pollens and the more common miscellaneous products, such as orris root, pyrethrum, flaxseed, silk and cottonseed, one may expect to ascertain the specific cause in about 33 per cent of cases. The contact tests, for substances known frequently to produce various dermatoses

Table 7

A STUDY OF THE FAMILY HISTORIES OF 128 PATIENTS WITH URTICARIA OR ECZEMA AS THE CHIEF COMPLAINT

Urticaria	Eczema	Age	Maternal	Paternal	Other Members
+		31	0	0	0
+		31	Urticaria	0	Son—Urticaria
+		32	Urticaria Migraine	0	0
+		32	0	0	0
+		32	0	0	0
+		32	Abdominal allergy	0	Brother—Urticaria
	+	32	0	0	Sister—Hay-fever
+		33	Urticaria Asthma	0	0
+		33	0	Asthma	0
+		33	Asthma	0	0
	+	33	0	Hay-fever	0
	+	35	0	0	0
+		35	0	0	0
+		35	Hay-fever Asthma Migraine Abdominal allergy	0	0
	+	35	Eczema	Asthma	0
+		36	0	Eczema	0
	+	36	0	0	0
+		36	Urticaria	0	0
	+	37	Asthma	0	Sister—Hay-fever
+		38	Fam. hist. unk.		
+		38	0	0	0
+		38	Migraine	0	0
	+	38	0	0	0
+		39	0	0	0

Table 8

A STUDY OF THE FAMILY HISTORIES OF 128 PATIENTS WITH URTICARIA OR ECZEMA AS THE CHIEF COMPLAINT

Urticaria	Eczema	Age	Maternal	Paternal	Other Members
+		40	Urticaria	0	Brother—Asthma
+		40	Hay-fever Urticaria	0	Son—Asthma
+		40	0	0	0
+		41	0	0	Daughter—Hay-fever
	+	41	0	0	0
+		42	Hay-fever	Asthma	0
+		43	Urticaria	0	0
+		43	0	0	Brother—Asthma
+		43	0	Urticaria	0
+		43	Hay-fever	0	Sister—Hay-fever
	+	43	0	0	0
+		44	0	0	0
+		44	0	0	0
	+	46	Asthma	0	0
+		47	0	0	0
+		48	0	0	0
	+	49	0	0	0
	+	49	0	0	Sister—Hay-fever
+		50	0	0	0
+		50	0	0	0
+		50	0	Asthma	0
+		50	0	0	0
	+	50	Hay-fever	0	Sister—Asthma
	+	51	0	0	0
	+	54	0	0	Son—Hay-fever
	+	54	0	0	Daughter—Urticaria

Table 9
A STUDY OF THE FAMILY HISTORIES OF 128 PATIENTS WITH URTICARIA OR ECZEMA AS THE CHIEF COMPLAINT

Urticaria	Eczema	Age	Maternal	Paternal	Other Members
+		54	0	Asthma	0
+		55	0	0	0
+		59	0	0	0
	+	60	0	0	0
+		63	0	0	0
+		65	Urticaria	0	Sister—Asthma Hay-fever
+		67	Asthma	0	0
+		74	Asthma	0	0

or for special substances indicated by the history, will bring out other specific etiologic factors. Still others can be found by the indirect or passive transfer method. Finally, in the absence of positive tests, a careful history will often suggest a specific cause. This is especially true of dermatitis medicamentosa. Proof consists in disappearance of symptoms following elimination of suspected substances and their reappearance on contact.

The nature of the condition to be investigated largely determines the method of testing to be employed; in some cases only one method is necessary, whereas in others two or more are required. Certain substances protein in nature may react better with one method, while others which are non-protein may react better with another. Bloch[2] states that in every case of chronic or acute eczema in his clinic, the so-called eczema tests rather than food tests are systematically employed; he considers the latter unimportant. If both are employed, however, certain eczemas will be found due to foods, particularly among patients in the first decade of life. As emphasized by Rowe,[9] common foods, such as wheat, eggs, milk, meat and potatoes, are more often responsible than foods seldom used.

The incidence of cutaneous manifestations of allergy has not been settled, and probably never will be, since the etiology cannot be determined in all cases. In the broadest sense of the term, all dermatoses may be considered allergic in that they represent altered reactions. Just how many eventually will be assigned to allergy, as we use the term, is a question which cannot be answered. It is encouraging to observe that some of the more conservative dermatologists appear to be discarding metabolic and other theories and to be favoring the principle of allergy. It is believed that further investigation, increased knowledge and improved methods will clear up the etiology of some of the dermatoses which are unexplained at the present time.

In conclusion, it is hoped that this discussion will help clarify rather than confuse the problems involved. One of the needs today seems to be a more general realization of the fact that certain dermatoses are allergic and consequently more frequent investigations along this line are needed, particularly in obscure cases.

In the past, many investigators who have become interested in allergy have discarded it; not because the principle is wrong, but because certain aspects are not clearly understood. Others have employed skin tests in a very superficial manner or have expected too much from the laboratory procedure, which is only a part of the investigation.

In this series, referring to those with a chief complaint of urticaria or eczema only, the average duration of symptoms before examination was five years. It behooves us, therefore, to adopt some practical attitude toward allergy in order that patients who can be benefited will receive relief without unnecessary delay.

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DISCUSSION (*Abstract*)

Dr. Walter J. Highman, New York, N. Y.—Dr. Henry uses the term "allergy" for altered reactivity in cells. This is precisely the same idea that Bloch had in mind when he redefined what he once called allergic manifestations. Now, it is a far cry, in using the term allergy in this restricted way from one in which the term is loosely used to define a clinical description.

According to Kolmer's idea the terminology has been refined to include all kinds of hypersensitivity, has it not? And we might as well, instead of having to apologize for the redefinition of a phrase, use an older

one, which is as broad as what Kolmer had in mind, when we remodel the new one. With this exception, which is purely a matter of terminology, I should say that Dr. Henry's presentation absolutely conforms with the philosophic and scientific aspects of the problem up to the point which we have reached in understanding it.

Dr. C. F. Lehmann, San Antonio, Tex.—Papers like this certainly tend to stimulate us in our study to determine the specific agent responsible for these sensitization cases. I feel that there is much work to be done in properly analyzing the whole subject of allergy. Of course we should persist in testing and in determining the specific sensitizing agents of our patients. But as big a field, and certainly to my mind the most important field in regard to this work, lies in searching for those things in the body that are what we would call predisposing factors. From the standpoint of therapy, this is the practical application of the whole idea, for to isolate a case or desensitize a case is usually impractical. But I prophesy that in twenty years we will be treating these cases by changing the individual so that his cells will not have the affinity against the particular agent. And without any criticism or disparagement of present day desensitization work (we all need to know more of it) I feel that we should study the patient just as diligently as we try to determine the agents to which he is intolerant. This search for predisposing causes is far in the background; and I think that along with such studies as have been exemplified by this paper, we should be studying the patient in an attempt to explain the underlying biological reasons for these phenomena.

Dr. Harry M. Robinson, Baltimore, Md.—For several years I have had a hand in the feeding of some of the babies in Baltimore who were sensitive to milk, and in many of these beneficial results were obtained by eliminating the irritating factor in the baby's dietary. In most of these cases the parents seemed healthy and denied skin or mucous membrane trouble. In following these children we have noted that some have been able to return to a normal diet including milk, butter and eggs without any idiosyncratic response, while others have continued to react, if not on their skin then on the mucous membrane, with asthma or hay-fever.

I should like to know in what way the factor of heredity would aid us in the treatment of these patients. The thing that seems to help most is the elimination of an idiosyncratic substance with which the patient is in contact.

Dr. Henry (closing).—We see children who are definitely sensitive to foods and it has been our experience that those who are sensitive to foods only sometimes desensitize themselves by abstaining from certain foods over a fairly long period of time and then taking only small amounts for a while. These are the ones who sometimes "outgrow" or overcome certain allergic manifestations such as eczema, urticaria or asthma. Other patients remain sensitive throughout life, however, and are never able to take certain foods.

Rackeman has prepared an interesting chart showing that during the first year of life food allergy plays a much more important role than inhalant; as age increases, however, food allergy decreases. On the other hand, other forms of allergy increase and at about the age of six years the lines cross, the food curve continuing downward and the inhalant upward.

NERVOUS DISEASES AMONG CHILDREN: A REVIEW OF ADMISSIONS TO THE CHILDREN'S HOSPITAL, WASHINGTON, D.C., 1925-1930*

By DANIEL D. V. STUART, JR., M.D.,
Washington, D. C.

Although studies have been made of many nervous disorders as entities in childhood, very little has appeared in print on the frequency of neurological diseases in general in children as a group. For a long time it has seemed to me that a study of such incidence would be interesting and perhaps revealing. As the preliminary step in a study of this character, and as the most practical way of obtaining reliable and probably representative statistics, a survey was made of the admission records of the Children's Hospital in Washington over a period of five years, from January, 1925, to January, 1930. Those cases having neurological diagnoses, primary or secondary, which were treated on the wards of the Hospital during that period, form the groundwork of the survey and the subject matter of this paper. This group represented house cases exclusively, the out-patient records not being included in the review. However, the cases seen in my own (neurological) division of the out-patient department were only such as form the clientele of any dispensary clinic. They will be, moreover, the subject of a separate report.

The Hospital contains 185 beds, 30 in private rooms, and 155 on the open wards. The constant population is approximately 60 per cent white and 40 per cent negro. During the five-year period under study, 17,476 cases were admitted; an average yearly turn-over rate of 3,527. The total figure, however, included over 6,500 children whom I have designated in *Table A* as "24-hour cases." This group comprised tonsillectomies and adenoidectomies, circumcisions and cast applications without operation. Many of these were discharged on the day of admission and the whole group was excluded as not hospital cases in the proper sense. This reduced the number of admissions to 10,949. Of this revised total of patients admitted, 736, or 6.79 per cent, were given neurological diagnoses: either primary, that is, as the condition

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Table A

SUMMARY OF ADMISSIONS
JAN. 1, 1925, TO JAN. 1, 1930

	All Services	Medical	Surgical
Total No. admissions	17,476	5,826	11,650
Eliminated '24-hr.' cases	6,527		6,527
Revised No. admissions	10,949	5,826	5,123
Total neurological cases	736	702	34
Primary	635		
Secondary	101		
Per cent neurolog. cases	6.79	12	0.66
Number of beds	185		
White	107		
Negro	78		
Av. yearly turn-over	3,527		

for which they required hospitalization; or secondary, as a complication of some other illness, or as an intercurrent disease. Subdividing the 10,949 admissions between the two major services, medical and surgical, an almost balanced proportion appeared on each, there having been 5,826 medical cases and 5,123 surgical. No such ratio, however, existed with regard to the neurological cases. Only 34 of the latter belonged in the surgical group, while 702 were medical. In other words, 12 per cent of all cases on the medical services during the period reviewed were of nervous diseases; a much higher figure than I had thought to find. The primary neurological diagnoses far outnumbered the secondary, there being 635 of the former to 101 of the latter. Tuberculous meningitis, although classified separately in the hospital records, is here placed in *Column III* of *Table B* (Diseases of the Meninges). In the 115 cases of tuberculous meningitis included in that column, I have considered the neurological diagnosis as primary, since all were admitted because of the meningeal condition, not the systemic lesions. For the sake of brevity I have made no tabulations of spinal fluid reports nor of the results of post-mortem examinations. In that connection, however, I may say that a routine spinal fluid examination was done on all patients on the neurological service, or seen by me or my associate in consultation; a total of 300 cases, approximately one-half of those listed in *Columns I, II,* and *III* of *Table B*. In all but 40 the fluid findings were in accord with the clinical diagnosis. A scattered number of spinal fluid examinations were made on the other groups in the table, with of course negligible results, excepting only the epileptics. Twenty-three of the 40 patients in this disease group were considered to have so-called essential epilepsy. Of these, 5 showed a definite increase in the spinal fluid pressure without other changes. This appears to be of some significance in view of late reports. Necropsy records when available showed the anatomical and clinical diagnoses to coincide in all but one instance. This was a case of tuberculoma of the brain, which had been regarded on the ward as tuberculous meningitis.

Table B

GENERAL CLASSIFICATION AND DISPOSITION, NEUROLOGICAL CASES

	Diseases of Brain and Cord (Exclud. Tumors)	Brain and Cord Tumors & Abscesses	Diseases of the Meninges	Diseases of the Peripheral Nerves	Amentia	Endocrinopathies	Epilepsy	Psychogenetic States (neuroses)
	I	II	III	IV	V	VI	VII	VIII
Total number	237	18	336	17	59	8	40	21
Recovered	30	1	35	5		2	4	9
Improved	102	2	23	3	5	2	12	4
Condition unch'd	80	2	108	8	54	4	23	8
Died	25	13	170	1			1	
Operation		11						
Necropsy	6	1	23					

Analysis of the figures in the first four columns of *Table B* brings out certain points which seem to me of interest.

Of the 237 cases of diseases of the brain or spinal cord, 77 were of acute or chronic encephalitis, using that term in its pathological sense, not as meaning a specific disease; 52 of acute chorea minor; 37 of acute anterior poliomyelitis; 16 of post-poliomyelitis paralyses or deformities; 27 of Little's disease; and 11 of the residua of infantile cerebral hemorrhage. The remaining 17 were of various conditions ranging from cerebral embolism to progressive muscular dystrophy (two cases); with one case each of myotonia congenita and cerebrospinal lues included. The last occurred in an infant of one year who had been under treatment in the luetic clinic of the hospital. Spinal fluid and post-mortem findings substantiated the diagnosis. In this column the outstanding features are: (a) the relatively high incidence of

Table C

ANALYSIS OF COLUMN I, TABLE B
Diseases of the Brain and Spinal Cord, Exclusive of Tumors and Abscesses

Encephalitis, acute and chronic	77
Acute chorea minor	52
Acute anterior poliomyelitis	37
Paralyses due to poliomyelitis	16
Little's disease	27
Infantile cerebral hemorrhage	11
Progressive muscular dystrophy	2
Cerebrospinal lues	1
Cerebral embolism	1
Miscellaneous	13
Total	237

encephalitis; (b) the very low proportion of acute poliomyelitis; (c) the number of cases of Little's disease; (d) the rather large group of choreics ill enough to require hospital care; and (e) the fact that many of the cases in the group gave a history of some one of the so-called children's diseases, antedating by only a short time the onset of neurological symptoms. This point seems most important.

Table D

ANALYSIS OF COLUMN II, TABLE B
Tumors and Abscesses of the Brain and Cord

A—Tumors	
Location not specified	7
Brain stem (medulla)	2
Cerebellum	2
Optic chiasm	2
Pons	1
Spina bifida	3
B—Abscesses	
Left temporal lobe (post-otitic)	1
Total	18

Column II is headed "Tumors and Abscesses of the Brain and Cord." The small number so diagnosed included, surprisingly, only one abscess, a post-otitic temporal lobe affair. Three cases of spina bifida placed in this group represented the only cord lesions. The entire group of 18, plus the 16 cases of deformities following poliomyelitis, a total of 34, were the only neurological cases on the surgical services. This is an unexpectedly low figure.

Table E

ANALYSIS OF COLUMN III, TABLE B
Diseases of the Meninges

Tuberculous meningitis	115
Pneumococcus meningitis	46
Epidemic cerebrospinal meningitis	42
Influenzal meningitis	29
Streptococcus meningitis	20
Undetermined or not specified	84
Total	336

In *Column III* there were, as has been noted, 115 cases of tuberculous meningitis. Forty-six cases of untyped pneumococcus meningitis occurred in this group; 42 of epidemic cerebrospinal meningitis; 29 of the influenzal type of infection; and 20 streptococcus cases, with the remainder undetermined or not specified. The very great proportion of meningeal tuberculosis is accounted for by the large negro population in the hospital (approximately 40 per cent) with the high tuberculosis rate of that race. No exact tabulation of figures was made, but the ratio of negro patients with this disease to whites was about 3 to 1. Pneumococcus meningitis ranked higher than, in my opinion, it should have; but not sufficiently so to be remarkable. The other types designated fell within expected limits. As regards the unclassified types, many of the cases had a history of acute systemic illness just prior to the development of symptoms of meningeal involvement, a point to be borne in mind in connection with the cases in *Column I*.

Table F

ANALYSIS OF COLUMN IV, TABLE B
Diseases of the Peripheral Nerves

Diphtheritic paralysis	7
Duchenne-Erb paralysis	3
Herpes zoster	1
Toxic neuritis	6
Total	17

Column IV included 7 cases of diphtheritic paralysis; 3 of Duchenne-Erb paralysis; and 1 of herpes zoster; the remaining 6 being peripheral toxic neuritides. The whole group is decidedly smaller than might reasonably have been looked for.

The figures in the last four columns (V to VIII) of *Table B* are not especially noteworthy. The fact that 59 cases of feeble-mindedness were admitted to the wards of a general hospital should, however, be explained. All but 9 of these patients were seen by me, though none was on my service. All had systemic illnesses of various sorts, but in all the mental picture was overshadowing. In 35 of the number, there were definite evidences of some previous organic brain disease, and this leads to the assumption that the mental defect was not inherent at all, but due to the brain damage. Again, as in tuberculous meningitis, our colored population rated higher; forty of the cases being negroes, nineteen white.

Column VI, the endocrinopathies, was made up wholly of thyroid disturbances. Three cretins, two patients with myxedema, and three hyperthyroidisms comprised the group. No doubt, cases of other types of glandular dysfunction were present on the wards during the period reviewed, but they were not so diagnosed.

In *Column VII*, all cases regarded as epileptics were listed; whether they belonged in the so-called essential subgroup, or were frankly symptomatic. This accounts for the comparatively large number hospitalized.

Finally, *Column VIII* is self-explanatory. In view of the fact that the psychoneuroses and emotionally determined states in general are

now commonly recognized in children, the number of cases in this column is not unduly large.

This paper has already been referred to as the preliminary step in a study of the incidence of neurological diseases in childhood. As such, it is intended only to give an outline of conditions as they exist in a general hospital for children, a sort of airplane view of the situation. In the consideration of the figures in *Table B*, however, a number of points of interest and significance are brought out which may be pointed out at this time, and which are well worth the detailed study that I expect to give them: the decidedly high percentage of nervous system disease in proportion to the total number of admissions on the medical service; the great preponderance of inflammations of the brain and spinal cord and the meninges, specifically the high proportion of encephalitis and meningitis cases of various types, and of probable post-encephalitic and meningitic states; the possible relationship of prior throat and ear infections to central nervous system disease, especially streptococcus meningitis; the question of how many patients with pneumococcus meningitis had lung involvement, and of what type of the organism is most often found in meningeal invasion; the whole matter of amentia and of epilepsy and the very important question of how often these conditions are apparent entities and how often the aftermaths or accompaniments of other disease processes. Each of these is a point of departure for investigation, possibly along quite new lines.

The records of the out-patient department of the hospital will be reviewed in another paper later on. They should also open up lines of inquiry. For example, the types of cases seen in the neurological clinic again emphasizes the possible role of central nervous system disease in the causation of various mental and physical disturbances. These cases on casual review fell into five main groups: first, the unquestionable after effects of encephalitis, meningitis, infantile cerebral hemorrhage, and so forth; second, the epilepsies; third, chorea; fourth, the ill-defined group of the endocrinopathies; fifth, the aments.

To sum up the high lights of this short survey as I see them:

(1) Organic nervous disorders, either as entities or as a complication of systemic diseases, are much commoner in children than physicians generally seem to think.

(2) A clear recognition of this fact should better both mortality and morbidity statistics, and should also lead to a therapeutically more helpful attitude toward conditions over which shoulders are now hopelessly shrugged, notably the sequellae of inflammatory diseases. After all, patients consult physicians with a view to treatment. They are not primarily interested in diagnostics.

(3) A neurological service has a definite place in the staff organization of a children's hospital, and the neurologist on duty should be called, not occasionally, but routinely as a consultant in all cases showing symptoms or findings referable to the nervous system. I do not mean that all such cases should necessarily be put on the neurological service; but that they should be seen by the neurologist. With all due respect, he is better trained than any one else in the early recognition and treatment of nervous diseases, or else he is not worthy of his title.

DISCUSSION (*Abstract*)

Dr. John A. Foote, Washington, D. C.—A statistical paper points out trends which we cannot get in any other way.

I had the pleasure a few months ago of hearing Dr. Flexner discuss the phenomena occurring in this country of increasing preponderance of inflammatory diseases of the brain and spinal cord. He pointed out the fact that not only was epidemic meningitis increasing, but also that an entirely new disease had appeared not heretofore known or recognized, which we call encephalitis. This, with increased poliomyelitis and various other forms of meningitis, showed a marked increase during the last quarter of a century in the United States. This is borne out in Dr. Stuart's investigation at the Children's Hospital in Washington.

In the admissions at this hospital there were 46 cases of pneumococcus meningitis. Meningitis occurs especially in childhood among negroes.

Dr. A. L. Skoog, Kansas City, Mo.—I should like to ask whether Dr. Stuart has any statistics bearing upon the incidence of influenza following encephalitis.

Among the encephalitis cases, did he encounter many of the sub-acute or chronic types? I believe there are many cases of a vague, chronic encephalitis that are unrecognized, particularly as we see them among adults rather than among children.

I should like to add also that possibly the term "amentia" might be criticised as used here.

Dr. Carrol Turner, Memphis, Tenn.—I was struck in Dr. Stuart's statistics with the small percentage of tumors over a period of five years. I think, if I remember correctly, that there were 18; and of that 18 only two cerebellar tumors. And also, his high percentage of amentia, 59; and epilepsy classified just as epilepsy, 40. I wonder whether some cases of so-called amentia were not organic brain diseases, probably tumors. We commonly see cerebellar tumors in children.

Within the past year we have had five in the Memphis General Hospital.

Not until a child develops all kinds of cerebellar pressure, or unless it shows some proven symptom, does the pediatrist usually call a neurologist.

Dr. Stuart (closing).—Dr. Skoog asked how many of the unusually high proportion of acute encephalitis cases followed influenza. It was practically impossible to get any statistics on that score, so I purposely did not try to venture a guess. A large proportion of these cases were negroes and their histories are unreliable. They call everything "flu." If a child has had anything from a coryza to a pain in the abdomen, they say, "Oh, yes, Doctor, he had flu a month ago."

About 20 of the total number had been previously seen in the medical clinic of the out-patient department and treated there for respiratory infection.

Dr. Skoog also made the remark that there were probably many vague unrecognized cases of encephalitis. That was one of the points I tried to bring out in my paper. I am quite sure of that. I used the term "amentia" for the sake of brevity. It always struck me as being a useful one, especially in contradistinction to dementia.

I do not know how to explain the small percentage of tumors. In my own dispensary I have made a positive diagnosis of brain tumor myself in no less than eight cases in the past two years. I tried to hospitalize the cases, only to be refused by the parents. I have not been able to follow the patients. As for the amentias or the feeble-minded in the hospital, I am quite sure the ones I saw did not have brain tumors, but I am by no means sure they were true amentias, that is, that they were congenitally feeble-minded individuals.

THE PERIODICAL SEASONAL INCIDENCE OF GASTROINTESTINAL SYMPTOMS COMPLICATING RESPIRATORY INFECTIONS IN CHILDHOOD: SEASONAL GASTROENTERITIS*

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During the past eight years the periodical seasonal incidence of gastrointestinal symptoms complicating respiratory infections in childhood has been true to type, both clinically and seasonally each year. In 1928, 92 of these cases were reported, 79, or 84.6 per cent, occurring in the months of January and February.[1]

Year after year the cases are true to type clinically and more so seasonally, and in the majority of cases they are as easily diagnosed as measles, whooping cough or scarlet fever. The variations in the clinical manifestations are no greater than in the above diseases.

The disease is characterized by either nausea, vomiting or paroxysmal abdominal pains. Drowsiness, dehydration and embarrassment to respiration are among the most constant symptoms.

The children are apathetic, their movements are slow and listless. The respiration is slow, a little labored, shallow and abdominal in type.

The patient is pale, the eyes are sunken, expression pinched and anxious. There is an acetone odor to the breath. The mouth is dry and parched. The tongue is coated, throat often congested or inflamed. In a small number of cases there may be a cough or bronchitis.

Many are drowsy and sleepy, but a few are restless, rolling the head from side to side.

The children have little or no fever. Many are constipated, but in some there is a diarrhea.

There is rapid loss in weight. Collapse and prostration are out of proportion to the apparent illness of the child.

In the older children the symptoms are milder. They complain of paroxsymal abdominal pains, are nauseated and often vomit. There may be either constipation or diarrhea.

The severe cases among the younger children, especially condensed milk babies, present all the clinical manifestations and physical findings of so-called alimentary or intestinal intoxication.

We have seen the classical text book picture of the

"open mouth, sunken eyes, fixed and glassy stare, the skin having the peculiar gray pallor of wet ashes, being dry and lacking in elasticity and remaining in folds when picked up. The hands and feet are cold and clammy. When aroused the child gives a shrill and piercing cry. There is marked air hunger and often an enlarged liver. Many of the cases are in deep coma, convulsions and vomiting of a coffee ground material are not unusual."

The children may have a diarrhea, but often are constipated with persistent and marked abdominal distention.

During the first twenty-four hours of the illness the urine invariably shows a heavy acetone reaction and the neutrophilic percentage increase is out of proportion to the increase in the number of white blood cells.

The 235 cases to be reported for lack of a better name will be called seasonal gastroenteritis. They were seen in private practice be-

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tween September 1, 1922, and September 1, 1930.

The age of the children follows:

21 cases under one year of age
58 cases between 1 and 2 years of age
46 cases between 2 and 3 years of age
110 cases over 3 years of age

Approximately 60 per cent of the patients either had a respiratory infection at the time of the illness or gave a history of an infection a few days prior, or developed symptoms and signs of an infection during the time or a few days after the illness.

In a certain number of the patients showing no signs or symptoms of a respiratory infection, it is not unusual to find other members of the family with respiratory infections.

During the time of the illness 6 of the 235 patients had symptoms or signs of an otitis media. Five were found to have had a pyelitis. Six developed signs and symptoms of appendicitis. They were all operated upon within 12 hours of the first appendical symptoms and in each case was found an acute gangrenous appendix. The ages of these children were: 18 months, 33 months, 39 months, 6 years and two cases 9 years of age.

They all made a good recovery.

The period of incubation in seasonal gastroenteritis is apparently of short duration, two to five days.

The number of contacts who contract the disease is greater than those from scarlet fever, but considerably less than from measles and whooping cough.

Our records show that in only 12 of the 235 cases was the diagnosis made more than once in the same patient.

Seasonal Incidence.—During the 8 years in which the 235 patients were observed, 150, or 64 per cent, were seen during the months of January and February.

The yearly percentage incidence of occurrences in January and February over the 8-year period is given in *Table 1*, the percentage of occurrences of the total number of cases each year varying from 51.6 to 95.

Seasonal gastroenteritis is more of a seasonal disease than either whooping cough, measles, scarlet fever or exanthem subitum, as occurring in private practice over the period of observation.

The four months in which the largest per cent of the total number of cases occurred in each of the five diseases follows:

Disease	No. Cases	Mo.	Per Cent	Mo.	Per Cent	Mo.	Per Cent	Mo.	Per Cent
Seasonal gastroenteritis	235	Feb.	34.4	Jan.	29.3	Dec.	9.3	March	8.9
Whooping cough	262	April	21.3	May	19	July	17.1	June	11.8
Measles	219	April	28	May	23	March	22.4	June	7.7
Scarlet fever	69	Dec.	16	Jan.	14.5	March	11.6	Nov.	8.7
Exanthem subitum	27	March	22.2	May	22.2	April	14.8	Dec.	11.1

In 224 cases in which a diagnosis of acute otitis media was made, the four months in which the largest per cent of the cases were seen follows: January 21 per cent, March 15 per cent, May 11.6 per cent, February 11.2 per cent.

TABLE 1

The Yearly Percentage Incidence of Occurrences in January and February of 235 Cases of Seasonal Gastroenteritis Observed During an Eight-Year Period

Years	1923	1924	1925	1926	1927	1928	1929	1930
Per cent of cases seen in January and February	72.3	81	87.5	77.7	55.5	95	51.6	52

Table 3 is an analysis of the leucocyte count and neutrophil percentage made in 38 patients with seasonal gastroenteritis with comparison of that of normal children[2 3 4] of the same age.

All counts included in this series were made within 24 hours of the beginning of the illness and were made on consecutive patients seen in 1929-30.

The lowest count was 5,500, the highest was 23,000, the average count per patient being 11,675. In 27, or 71 per cent of the children, the counts were below 13,000.

The lowest neutrophil percentage was 58, the highest was 95, average being 78.2. In 19, or 50 per cent of the children, the neutrophil percentage was above 80. In 31, or 81.5 per cent of the cases, it was above 70.

TABLE 2

The Monthly Percentage Incidence of the Number of Cases of Seasonal Gastroenteritis as Compared to the Number of Whooping Cough, Measles, Scarlet Fever and Exanthem Subitum Patients Seen in Private Practice Over an Eight-Year Period

Disease	No. Patients	Monthly Percentage Incidence of Occurrences											
		Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	March	April	May	June	July	August
Seasonal gastro-enteritis	235	0.8	2.9	6.8	9.3	29.3	34.4	8.9	3.4	1.7	1.3	0.4	0.4
Whooping cough	262	1.9	0.4	0.7	1.1	3.4	9.1	9.1	21.3	19.	11.8	17.1	4.2
Measles	219	1.3	0.4	0.9	2.3	4.5	7.3	22.4	28.	23.	7.7	0.9	1.3
Scarlet fever	69	4.3	13.	8.7	16.	14.5	10.1	11.6	3.	1.4	1.4	10.1	5.
Exanthem subitum	27	0.	3.7	3.7	11.1	7.4	7.4	22.2	14.8	22.2	7.4	0.	0.
Otitis media, acute	224	4.	6.2	8.	8.9	21.	11.2	15.6	8.4	11.6	4.4	3.7	1.3

TABLE 3

Analysis of Leucocyte Counts and Neutrophil Percentage in 38 Patients with Seasonal Gastroenteritis with Comparison to the Normal for Age[2 3 4]

	Total Leucocyte Counts				Neutrophil Percentages										Normal for Age	
Age in Years	No. Patients	High	Low	Average	Under 10000	10000 to 15000	15000 to 20000	20000 to 23000	High	Low	Average	58 to 70	70 to 80	80 to 90	Over 90	Leucocytes	Neutrophils
0- 1	4	11000	8000	9250	3	1	0	0	80	65	71.2	2	1	1	0	15000	30.4
1- 2	6	17000	6000	10333	3	2	1	0	93	61	77.8	1	3	1	1	14500	36.3
2- 3	4	13200	5500	8600	3	1	0	0	72	58	66.5	2	2	0	0	14000	38.7
3- 4	4	15000	7500	11125	1	2	1	0	90	58	76.7	1	1	1	1	13500	44.7
4- 5	5	21000	9000	13600	3	0	0	2	90	70	81.6	0	1	3	1	13000	48.5
5- 6	4	21000	10000	13250	0	3	0	1	91	74	82.7	0	2	1	1	12500	56.5
6- 7	1	11000	11000	11000	0	1	0	0	71	71	71	0	1	0	0	12000	56.
7- 8	3	20000	6000	12000	1	1	0	1	84	63	75	1	0	2	0	12200	54.4
8- 9	4	23000	12000	16000	0	2	1	1	95	81	92.6	0	0	1	3	12000	56.
9-10	1	12000	12000	12000	0	1	0	0	79	79	79	0	1	0	0	12000	57.
10-11	1	9000	9000	9000	1	0	0	0	88	88	88	0	0	1	0	11500	58.
11-12	1	12750	12750	12750	0	1	0	0	85	85	85	0	0	1	0	11000	60.
	38	23000	5500	11675	15	15	3	5	95	58	78.2	7	12	12	7		

Table 4 shows an analysis according to age grouping, with comparison to the normal count of children of the same ages in 38 cases diagnosed as seasonal gastroenteritis, and 21 cases of scarlet fever, 35 cases of whooping cough and 18 cases of exanthem subitum seen in private practice during an 8-year period.

The counts in seasonal alimentary infections and exanthem subitum were made on consecutive patients, while in scarlet fever and whooping cough the only counts included are the ones made on selected uncomplicated cases, showing a more or less typical blood picture of the disease.

The average blood pictures in the 4 diseases follow:

	W.B.C.	Neutrophil Percentage
Seasonal gastroenteritis	11,675	78.2
Scarlet fever	17,378	79.5
Whooping cough	20,877	27.
Exanthem subitum	9,144	29.8

COMMENT

The blood pictures in seasonal gastroenteritis were more characteristic than either whooping cough or exanthem subitum. With the exception of the increase in the number of white blood cells in scarlet fever, the blood pictures of that disease and seasonal gastroenteritis are very similar.

TABLE 4

The Leucocyte Counts and Neutrophil Percentage, According to Ages, in 38 Cases of Seasonal Gastroenteritis, Compared with 21 Cases of Scarlet Fever, 35 Cases of Whooping Cough, and 18 Cases of Exanthem Subitum.

	No. of Patients				Average Leucocyte Count				Average Per Cent of Neutrophils				Normal for Age	
Age in Years	Seasonal Gastroent.	S. F.	W. C.	Ex. Sub.	Seasonal Gastroent.	S. F.	W. C.	Ex. Sub.	Seasonal Gastroent.	S. F.	W. C.	Ex. Sub.	Leucocytes	Neutrophils
0- 1	4	0	10	4	9250		19575	7750	71.2		21.8	13.7	15000	30.4
1- 2	6	0	4	7	10333		23845	8585	77.8		27.2	24.2	14500	36.3
2- 3	4	1	6	4	8600	15000	24483	10562	66.5	74	23.8	33.7	14000	38.7
3- 4	4	5	6	1	11125	16000	21625	5500	76.7	82	25.3	59	13500	44.7
4- 5	5	3	2	2	13600	17000	22000	12875	81.6	73	23	59.5	13000	48.5
5- 6	4	2	3		13250	14075	15333		82.7	76.5	41		12500	56.5
6- 7	1	3	3		11000	21175	20585		71	86.7	38		12000	56
7- 8	3	1	1		12000	18250	12000		75	85	20		12200	54.4
8- 9	4	1			16000	28000			92.6	94			12000	56
9-10	1	5			12000	15410			79	74.5			12000	57
10-11	1				9000				88				11500	58
11-12	1				12750				85				11000	60
Total	38	21	35	18	11675	17378	20877	9144	78.2	79.5	27	29.8		

Our records show blood counts in scarlet fever as high as 60,000. In one case of whooping cough the count was above 120,000.

In seasonal gastroenteritis we have seen leucocyte counts above 50,000, but only in patients who were very toxic and showing signs of severe shock, the high count evidently being due to the dilatation of the superficial capillaries.

Hoff, Foldes and Sherman have shown that in an acidosis there is a relative increase in the myeloid cells, while in alkalosis there is an increase of the lymphocytes.

Heinsheimer[5] produced an artificial acidosis in rabbits and in men and found the percentage of neutrophils showing a definite and often marked increase. Immediately after the condition was produced there was a decrease in the number of white cells, there being an increase in the course of the next two hours, reaching the original count and often above at the end of five hours.

In the animals and men in which an alkalosis was produced there was not much change in the absolute count, but there was a drop in the percentage of neutrophils and a relative increase in the lymphocytes.

Marriott[6] and many other investigators[7 8 9 10 11] have repeatedly called our attention to a type of case in young children characterized by

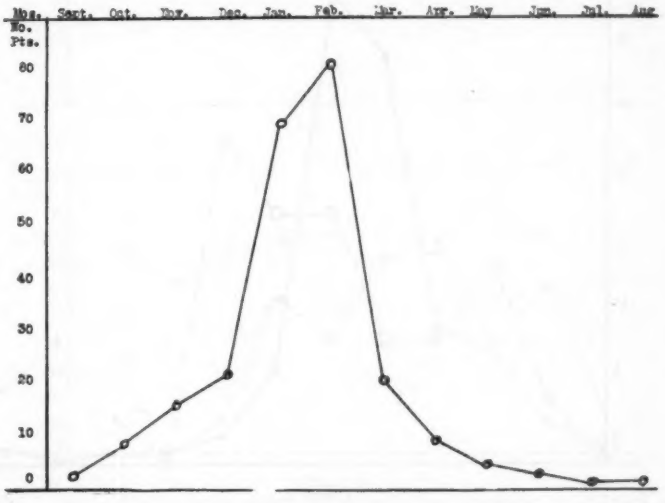

Chart 1

The monthly incidence of 235 cases of seasonal gastrointeritis, observed in private practice during an eight-year period. One hundred and fifty, or 64 per cent, of the patients were seen in the months of January and February.

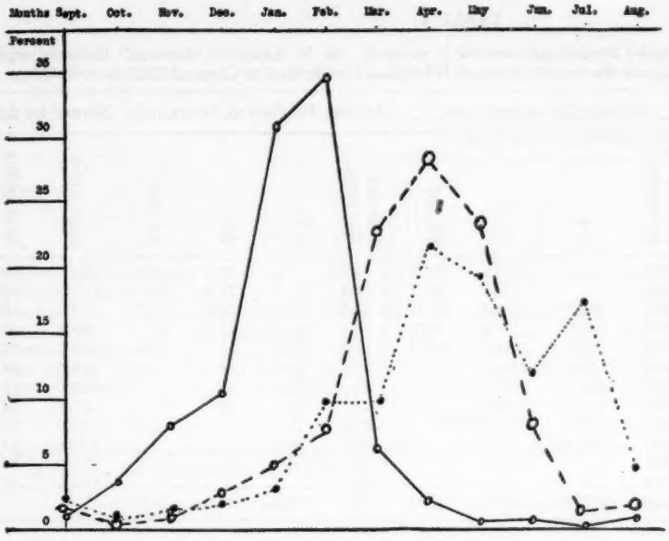

Chart 2

The monthly percentage incidence of occurrences in 235 seasonal gastroenteritis, 262 whooping cough and 209 measles, as seen in private practice during the same period of observation.

Solid line = Seasonal gastroenteritis
Dotted line = Whooping cough
Broken line = Measles

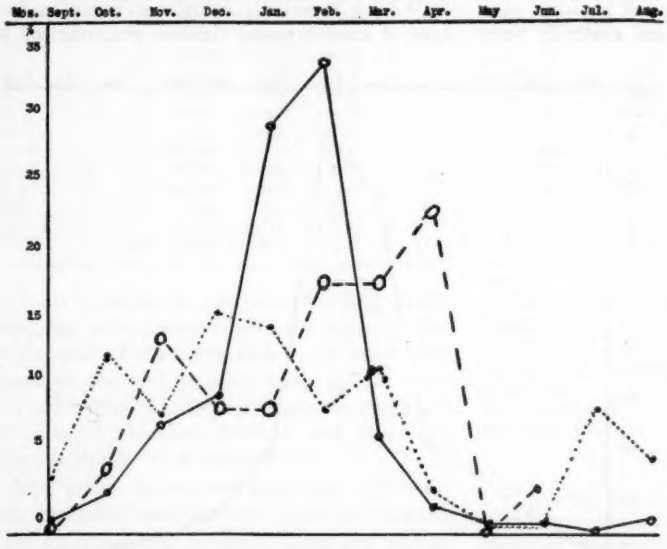

Chart 3

The monthly percentage incidence of occurrences in 235 seasonal gastroenteritis, 64 scarlet fever and 27 exanthem subitum patients, as seen in private practice during the same period of observation.

Solid line = Seasonal gastroenteritis
Dotted line = Scarlet fever
Broken line = Exanthem subitum

a severe gastrointestinal condition, vomiting and diarrhea with large watery stools, the stools containing mucus but no blood. There is a rapid loss in weight and increasing toxicity with marked dehydration.

These investigators are convinced that the symptoms are the result of a focal infection in the mastoid antrum and accessory nasal sinuses.

Marriott[6] summarizes the pediatric aspect of the symptoms in the following statement:

"The gastrointestinal symptoms are the result of a specific intoxication resulting from a streptococcus toxin and the toxin acts by damaging the capillaries of the gastrointestinal tract."

Brown[12] and his co-workers of Toronto, Canada, do not believe that the etiological factor in acute intestinal intoxication is an upper respiratory infection.

Brockman[13] reports 15 cases of what he calls influenza conditions, all cases being of remarkable consistency in general type and of a definite seasonal incidence.

The onset was sudden with vomiting of a bile stained material. There were severe abdominal pains, paroxysmal in type.

In one of the cases a diagnosis of intestinal obstruction was made and a laparotomy was done. He found the free fluid, the jelly-like lymph and the petechial hemorrhages that are commonly seen in these cases. In the lower portion of the ileum was a persistent contraction ring with distended bowel above and collapsed intestine below.

No organic cause of any nature could be found. He sug-

gested that the cause of the condition was an influenza toxin or some unknown virus associated with the disease causing a lesion of the posterior root ganglions.

The type of cases described by Brockman, in which the blood supply of the appendix is obstructed, might possibly explain our 6 cases of acute gangrenous appendicitis.

Freeman[14] reported 42 cases of appendicitis in children occurring during an epidemic of upper respiratory tract infections.

Seasonal gastroenteritis is a true ketosis.

Philip Cohen,[15] in reviewing the literature and reporting a series of cases showing various types of ketosis, states:

"There are three types of ketosis in childhood: (1) due to a depletion of carbohydrate reserve of the body by starvation; (2) the carbohydrate metabolism is abnormal. This type is always caused by infection and may be due to either one of two causes: a temporary pancreatic insufficiency or to a lowered hepatic function. (3) The third type is one where the blood sugar is normal, the carbohydrate metabolism is normal, glycosuria is present and infection is the cause."

Various authors have reported this same type of disease, calling it gastrointestinal grippe or intestinal influenza.

In 1928 we reported a series of these same cases under the name of "So-Called Gastrointestinal Influenza."[1]

In 1929, Zahorsky,[16] in reporting a series of cases observed in St. Louis, suggests that the disease be known as hyperemesis hiemis, or the winter vomiting disease.

We feel that the name suggested by Zahorsky is not a true description of the disease.

In a large per cent of our cases there was nausea, but little vomiting, the characteristic symptoms being: paroxysmal abdominal pains, prostration out of proportion to the apparent illness of the child, dehydration and embarrassment to respiration, the urine invariably showing a heavy acetone reaction, neutrophilic percentage increase being out of proportion to the increase in the number of white blood cells.

MANAGEMENT

The condition is a true ketosis and should be treated accordingly.

Water and cracked ice are given freely. In the constipated patients who vomit and are unable to retain anything by mouth, the amount of fluid that is absorbed by rectum in the first 24 hours of the illness is surprising.

In many cases it is necessary to give normal saline subcutaneously and intraperitoneally.

In every case glucose is given by mouth, rectum, subcutaneously or intravenously, according to the indications and conditions of the patient.

Orange juice in combination with glucose or plain water is given freely. The older children are offered toast and cooked cereals.

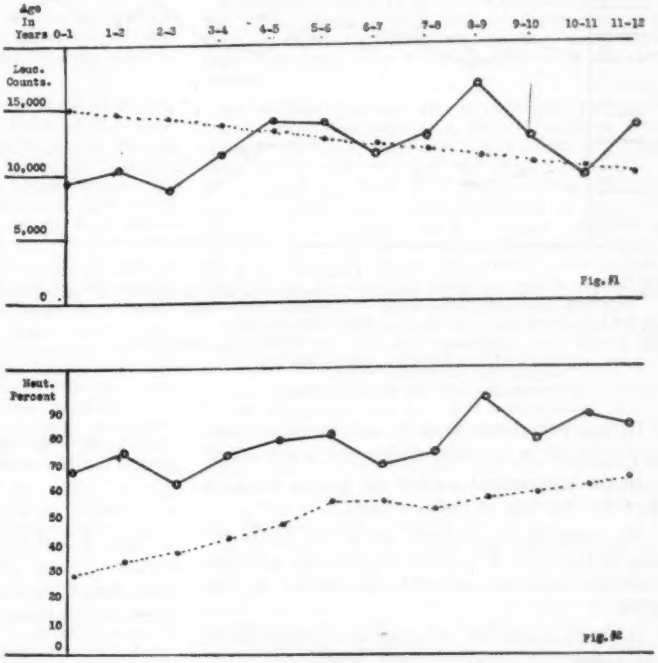

Chart 4

Fig. 1 (top). The leucocyte counts, according to age grouping, in 38 cases of seasonal gastroenteritis, with comparison to the normal counts in children of the same age.

Fig. 2 (bottom). Comparison of the percentage of neutrophils.
Solid line = Seasonal gastroenteritis
Dotted line = Normal children

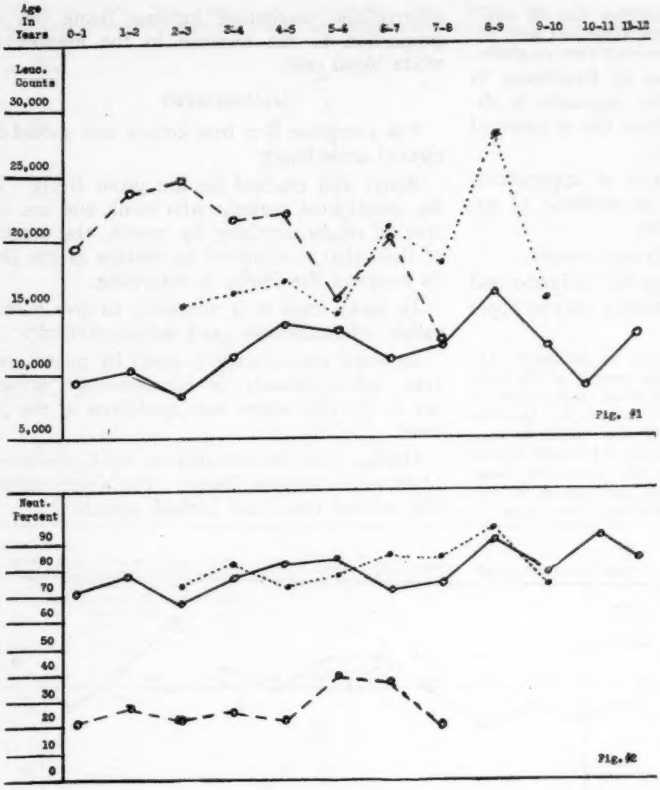

Chart 5

Fig. 1 (top). The leucocyte counts, according to age grouping, in 38 cases of seasonal gastroenteritis, with comparison to counts made in 21 cases of scarlet fever and 35 cases of whooping cough.

Fig. 2 (bottom). Comparison of the percentage of neutrophils.

Solid line = Seasonal gastroenteritis
Dotted line = Scarlet fever
Broken line = Whooping cough

In our experience milk in any form, as well as purgation, is harmful during the acute stage.

In the constipated patient the bowels are kept open by the use of soda enemas.

As a routine the patients are given alkali, the size of the dose depending on the age, physical condition and the amount of acetone in the urine.

In severe cases the transfusion of whole blood has apparently been of great benefit.

SUMMARY

(1) In an analysis of 235 patients seen in private practice over an eight-year period, with gastrointestinal symptoms, it was found that approximately 60 per cent were associated with a respiratory infection.

(2) The most characteristic symptoms were either nausea, vomiting or paroxysmal abdominal pains. There was drowsiness, dehydration and embarrassment to respiration. Prostration was out of proportion to the apparent illness of the child.

(3) During the first 24 hours of the illness the urine invariably showed a heavy acetone reaction and neutrophilic percentage increase was out of proportion to the increase in the number of white blood cells.

(4) The condition is more of a seasonal disease than is whooping cough, measles or scarlet fever. Of the 235 patients, 150, or 64 per cent, were seen in the months of January and February.

(5) The condition is evidently a definite entity. The gastrointestinal symptoms are probably caused by some unknown specific toxin or virus associated with the disease, acting directly or indirectly on the alimentary tract.

(6) Seasonal gastroenteritis is the name suggested for the condition.

CONCLUSION

The type of case reported has many, and in certain young children all, the characteristic signs and symptoms of so-called alimentary or intestinal intoxication.

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DISCUSSION (*Abstract*)

Dr. J. Mac. Bell, Mobile, Ala.—If we pediatricians knew all about the influenza bug, about 90 per cent of our troubles with children would be over, particularly in the winter months.

Dr. McLean reports a peculiar type of blood picture, which is observed quite early. I know of no condition that presents that picture early in the disease. The percentage of neutrophils in the blood is clearly out of proportion to the leucocyte count. I have observed this condition in several instances in cases which I labeled ketosis or acid intoxication or food intoxication.

I believe the condition described occurs throughout the winter months. I have also seen it twelve months out of the year.

The diagnosis which I have to depend upon in the mild type of case, the case that recovers in the first twenty-four or forty-eight hours, has been one of acid intoxication or food poisoning. That is the case with the severe blood picture. The severe cases that run along for several days and develop some respiratory symptoms peculiar to this particular bug, I have called influenza complicating ketosis or acidosis.

I should like to ask Dr. McLean what, if any, changes there are in the blood chemical findings, and what are the necropsy findings? Possibly we are dealing with an allergic manifestation due to a strain of the organism of influenza.

Dr. John Zahorsky, St. Louis, Mo.—Possibly this syndrome is the same that I described several years ago under the title of the winter vomiting disease, or hyperemesis hiemis. In a paper under that title I described these peculiar epidemics that occur in the winter time. Such an epidemic lasts about two weeks. Associated with them are, of course, the respiratory infections, which are generally present at that time. In my series, I believe, there were only about 40 or 50 per cent of respiratory infections. This peculiar syndrome, which occurs in the winter months and which I call the winter vomiting disease, seems different from ordinary gastrointestinal disturbances associated with the ordinary grippe. First, it occurs during a short period of time, two or three weeks. The symptoms are vomiting, sometimes constipation, often diarrhea with very foul and offensive stools. Dehydration and acidosis are common. This peculiar syndrome occurs during the winter months, and I am sure it is not entirely dependent upon the respiratory affection.

Dr. Lewis W. Elias, Asheville, N. C.—Dr. Ward and I saw between 50 and 75 very similar cases last winter, in February and March, lasting over a period of about eight weeks. They resembled the condition described by Dr. Zahorsky.

Dr. D. Lesesne Smith, Spartanburg, S. C.—The disease seems to be due to an upper respiratory infection. Upon careful examination of the throat the most marked and frequently the only lesion discernible is a granulated inflammatory condition of the uvula. This is present in the majority of the cases of the vomiting type.

The disease comes on in epidemic form, most often in January, February and March, but we see it during any month in the year.

The epidemic seems to be very widespread and covers the whole South. I have had telephone calls from Alabama, North Carolina, South Carolina, and Georgia about these cases when I had an epidemic in my own territory.

Dr. McLean (closing).—In my experience the condition described has more of a seasonal incidence than measles, whooping cough or scarlet fever, but cases were seen in each month of the year.

The blood picture of the condition is as typical as that of scarlet fever, whooping cough or exanthem subitum. It is evidently due to a ketosis, the duration of the picture depending on the duration of the ketosis. No blood chemical analyses were done on the patients reported, but the literature is full of reports of analyses of the same type of case by various investigators.

Two deaths occurred in malnourished condensed milk babies. Of the 235 cases reported, only 21 of the children were younger than 12 months of age.

In a recent epidemic of food poisoning in Chicago, Jordan found that the food was contaminated with a yellow staphylococcus. This organism, when grown in broth, produced a toxic substance. This substance, when passed through a sterile filter and swallowed by human volunteers, gave rise to nausea, diarrhea and prostration of the same character as that observed in the individuals with the food poisoning.

In my patients I have seen the type of throat described by Dr. Smith. In many, who apparently have no signs or symptoms of a respiratory infection, if a careful examination is made, evidence of a paranasal sinusitis will be found. The tongues of these patients have a dirty, greyish white coat. If the child is gagged and made to contract the muscles of the nasopharynx a mucopurulent discharge will be seen.

I feel sure that the type of case described by us is the same condition as Dr. Zahorsky's winter vomiting disease, but in many of our patients vomiting was not the characteristic symptom. There was nausea, dehydration, embarrassment to respiration, drowsiness and

in certain of the older children, paroxysmal abdominal pains.

The urine invariably showed a heavy acetone reaction, the blood showing the neutrophil percentage increase out of proportion to the number of white blood cells.

X-RAY THERAPY: OBSERVATIONS BASED UPON THE TREATMENT OF SIX HUNDRED CASES*

By E. C. THRASH, M.D.,
and
W. POPE BAKER, M.D.,
Atlanta, Ga.

Our chief purpose in presenting this subject is to broaden the scope of x-ray therapy in the minds of the general profession. This means of treatment has so long been associated with neoplasms that the average physician has a tendency to think of it only in terms of cancer. In reality the treatment of this malady is of minor importance compared to the great number of other diseases that are benefited and cured by x-ray therapy. Many radiotherapists themselves have not fully grasped the magnitude of this work. There is always a tendency to disparage and discount things new and not understood, and men trained in roentgen treatment have been more or less timid, and have not shown sufficient aggressiveness. The surgeon himself is so enthusiastic in mastering and perfecting his own technic that he does not make a sufficient study of the help he might get outside the operating room. With the radiotherapist's knowledge of the behavior of roentgen rays he can say to the surgeon that these rays are to the cells what the knife is to the tissues. The surgeon's knife is the macroscopic adjustor and adaptor of tissues for beneficent purposes, while the roentgen ray in proper hands is a microscopic implement that plays the same part with individual cells. Humanity will not be properly served until these two factors are understood equally and correlated.

One should approach this field of therapy with fear and trembling. To be a master, one must know physics, have a grasp of radioactivity, know as much as is known about the action of the rays upon cells, know the limitations and capacity of his individual machine, and the pathology of the diseases which he treats.

A proper grasp of radio-resistance and radio-sensitiveness is one of the most important factors in this field. Recent studies of x-rays in relation to chemistry, and especially crystallography, may open up a way by which we shall better understand the action of the rays upon cell structures. It is conceded that only the rays that stop in and are absorbed by the cells are effective in making chemical or biological changes. It is the opinion of physicists that these rays are stopped only by the electronic and co-electronic portion of the atom, and when a sufficient number of them is stopped by the electrons in the atom there are changes in atomic behaviors. The long waves have less chance to pass between a great number of electrons than the shorter ones do, so the short waves penetrate deeply before they are finally stopped, while the longer ones are stopped nearer the surface. This action changes the biologic behavior of the cells affected and is responsible for our results. These phenomena probably have some bearing upon radio-resistance. Without a definite knowledge, however, of the reason why, we do know that adult tissues of all kinds show greater resistance than do embryonic ones, and those cells which nearest approach the class of embryonic types show proportionately a greater radio-sensitiveness.

Squamous epithelium is quite radio-resistant, therefore neoplasms developing from these cells show the same characteristics, while the Malpighian layer is less resistant and is more readily acted upon by the rays. Fibrous tissue, muscle structure, bone and highly differentiated cells such as neurones are also resistant. The gland and mucous epithelium and endothelium might be considered the secondary group with reference to resistance. The cell structures that are less differentiated would be placed in the lowest class. Thymus cells, lymphocytes, parenchyma cells of the testes and ovaries are in this group. The red cells are resistant, and the granulocytes are more resistant than the lymphocytes. One must take all these facts into consideration when he treats any pathological process, bearing in mind that neoplastic cells developing from any of these structures conform in a measure to the behaviors of their parent tissues.

Artificial resistance caused by long-continued treatment should be borne in mind. The cells have a tendency to acquire an immunity against

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the rays and unless one gives the proper dosage as quickly as is practicable, a resistance will be established. There is a pseudo-radio-resistance which occurs when radio-sensitive neoplastic cells are encased in radio-resistant structures. This is especially the case in bony tumors. Often this class of tumors may be treated with the x-ray without apparent results, while a biopsy will show that the cancer cells have become inactive and have no tendency to infiltrate or otherwise disturb the surrounding tissues. This type should be handled with care, since over-treatment will cause cystic changes and weakening of the bony structures, with a tendency for them to fracture. Another class of pseudo-resistant neoplasms is that in which the neoplastic cells are in a heavy connective tissue framework. This class of tumors will show little reduction in size under treatment, or probably no reduction; the reason of which is that the fibrous tissue stroma has not been affected, while the parenchyma cells of the cancer have been either destroyed or put in a state of arrest. Many of these tumors have been over-treated. The fibrous tissue tumefaction may remain harmless indefinitely, but surgical intervention often sets the encapulated cells free and dire results ensue.

The accurate measurement of dosage has not as yet been solved. Many methods are offered that are not practical for the average operator, and even from a theoretical standpoint all of these have their intrinsic faults because of the variability of the factors involved. If the amount of energy could be calibrated with perfect accuracy, the equation of the individual treated would always be an insoluble variant. So, for the present at least, our dosage should be based upon the average amount of radiant energy required to produce certain results, calculated from the combined experience of the outstanding men in the work. This average dose with which we are all familiar should be used as a working basis, observing its effect upon each individual and making such modifications as are necessary. One should not be so timid as to fall far below the optimum dose, because harm may be done by the establishment of a radio-resistance. Where one wishes, however, to be more nearly accurate in the amount of radiant energy administered, our suggestion would be to make three ports about 1 cm. in diameter and two inches apart, giving a 75 per cent dose into all three of these ports, screen one port and give 25 per cent, then screen the second port, leaving one open, and give 25 per cent more into the third port. Observe these areas a week to ten days later and estimate the optimum dosage from the reaction.

We shall deal with radiotherapy by considering its effects upon individual cells and think of what we wish to accomplish in dealing with these. The cell groups which the radio-therapist handles are those that enter into the production of neoplasms, those that develop hyperplasias (Hodgkin's disease, enlarged thymus, lymphopathies, and so forth) and those entering into the activities of inflammatory processes. The lethal and paralethal dosages are used in neoplasms and hyperplasias, the mild reactionary doses in inflammatory processes.

Lethal doses should be used cautiously and they should be confined to small areas where the breach is not so wide that the surrounding tissues cannot repair the disturbance with a normal scar. Radium and fulguration will often better serve this purpose. When a lethal dose from the roentgen rays is administered the destruction is often too extensive and a profound shock is produced in normal tissues. In destroying tissues one must take into consideration that the surrounding normal cells must have sufficient vitality left and be near enough to all the destroyed area to set up a process of repair and replace the destroyed structure with a patch.

In treating large areas one should attempt to attain the happy medium of arresting the activities of all diseased cells and not minimize the shock upon normal physiological ones that are intermingled in a fibrous tissue network, holding in the meshes of this network the parenchyma cells of the neoplasm or hyperplastic disturbance. In other words, check and arrest the growth of the parenchyma cells and leave the fibrous tissue stroma in normal condition for the purpose of encapsulating the pathological cells whose growth has been arrested and fill the vacancies caused by the absence of these cells by fibrogenesis. One's purpose should be to destroy only the parenchyma of the tumor, leaving the framework to convert the malignancy into a fibrotic mass. A dose sufficient to shock severely the normal physiological cell content (fibrous tissue cells) so that it cannot react in a reparatory way to establish a connective tissue framework to take the place of the pre-existing pathological structures, would be pernicious.

We have concluded from our experience that lethal dosages or even the repeated bombard-

ments of the tissues with paralethal ones in the treatment of large malignancies often does harm and even hastens the death of the patient, while paralethal dosages sufficient completely to arrest the growth with no further treatment until there is evidence of the tumor's making further progress, is the optimum measure and will usually give patients several extra years to live. The condemnation of x-ray therapy has resulted almost entirely from over-treatment. The patient feels that in order to get well his tumor must be removed, and the physician himself is too enthusiastic in an effort to treat the patient until the tumor disappears. What should be desired is for the tumor to become hard and nodular with firm shrinkage. An arrest can often be brought about without even perceptibly diminishing the size of the tumor. This precaution should be borne in mind as well in treating metastasis as in treating the parent tumor. Heavy treatments for metastasis will injure the framework of the structures in which the neoplastic cells have been planted, leaving these tissues resistant and inviting greater extension of the metastasis.

In utilization of mild reactionary dosages of x-ray, the surface of the field has barely been scratched. There is more to be accomplished in non-cancerous x-ray therapy than in the treatment of cancer. There is only one step from ultra-violet rays to the wave lengths which produce x-rays, and their therapeutic effects are similar. The wave lengths that are just a little shorter than ultra-violet and which we can get only with the x-ray tube have wonderful therapeutic possibilities. These, properly controlled, will permit us to put therapeutic rays into the tissues instead of upon them, probably stimulating cell activities, but certainly bringing about metabolic changes that are beneficial to the general economy.

Only a brief summary of our 600 treated cases can be made. In this list are included all forms of neoplasms in all parts of the body, and many other pathological conditions, including Hodgkin's disease, leukemia, thymus enlargement, cystitis, and thyroid dyscrasias, acne, eczema, epidermophytosis, lupus, ringworm, hayfever, boils, carbuncles, sycosis, and many other skin lesions; bacterial endocarditis, hemorrhagic endometritis, tuberculosis of the larynx, tuberculous lymph nodes, sciatica, neuritis, tuberculous peritonitis, Reynaud's disease, various chronic infections, bronchial asthma, and bronchiectasis.

We wish particularly to emphasize the value of radiotherapy in treatment of pulmonic disturbances, especially in children. Tracheobronchial adenophathies caused from whooping cough, measles, tuberculosis and other respiratory infections respond especially well, and we know of no other treatment equal to this for such maladies. The senior author has wrestled with the problems of asthma for an interminable period with efforts resulting largely in disappointments. His conclusions now are that radiotherapy in bronchial asthma gives better results than other means of treatment. The complex known as hay-fever responds especially well. Patients treated who had been temporarily benefited with pollen vaccines have remained well. We have patients in whom the disease has remained quiescent for two years. The analgesic effect of x-ray treatment should be mentioned. Neurologists have referred us numbers of cases with intractable pains that have shown improvement following treatment over the nerve roots. This is especially true of sciatica. Pains from tumor metastasis have yielded very satisfactorily. Pains from phlegmonous inflammation, abscesses and boils are usually relieved. We have had one rather unusual case.

A man, twenty-two years of age, suffering from familial jaundice with greatly enlarged spleen, emaciated and able to do but little work, has had one series of treatments which was completed about a month ago. His hemoglobin was 60 per cent; it is now 65 to 70 per cent. His color has improved. He is very happy and has been at work since he got over the shock of the treatment. He came in a few days ago with a statement that he had made money enough to pay his bills since the treatment. This is *prima facie* evidence that we produced results.

We have treated quite a variety of brain tumors for Dr. Charles E. Dowman. We quote him as follows:

"To summarize, my impression is that the only intracranial tumors which may be cured with the roentgen ray are the pituitary hyperplasias and the medulloblastomas. The low grade malignant sarcomas of vascular origin may be cured by such treatments. With the exception of the pituitary hyperplasias I believe that all intracranial tumors should be investigated through operation and removed if possible, either totally or partially. I follow operations with roentgen-ray treatment in all cases of infiltrating tumors, metastatic carcinomas, and the sarcomas of vascular origin."

There is a vague impression among many physicians that deep therapy is a distinct method of treatment, disassociated from that with the softer rays. One's plant should have a sufficiently wide range to administer rays from the softest to the hardest that can be practically

used, ranging from 80 to 200 kilovolts. The problem confronting the therapist in every instance is, what is the average depth of the pathological tissue beneath the skin? What is the class and condition of the tissues with which he is dealing? What number of ports of entry would be practicable? What should be the degree of hardness of the rays in order to plant the maximum amount of radiant energy into the tissues treated with a minimum degree of skin disturbance? The proper solution to these problems will give good results in roentgen ray therapy.

DISCUSSION (*Abstract*)

Dr. V. W. Archer, University, Va.—In a patient who is in poor condition we should start off very carefully, attempting to check bleeding, so that he can get more blood into his system to increase his resistance to radiation. If we radiate, for instance, a lymphoblastoma too heavily, we shall cause the death of the patient. We should size up our patients to determine what they can stand, not judge our dosage merely from the pathological lesion with which we are dealing.

First of all, we should decide whether we are going to try palliation or a more or less permanent arrest of the process. I have no doubt that a good many persons' lives have been shortened by excessive doses of radiation when they were not in a position to stand it. A smaller dose at the start could have brought the patient's condition up, so that massive irradiation could have been tolerated.

Dr. Fred O. Coe, Washington, D. C.—There are very few people throughout the United States who are giving heavier doses of radiation than Dr. Merritt. In deep therapy for cancer, you have to realize that you are dealing with cancer to kill it, and in many cases you must nearly kill the patient to kill the cancer. I have seen that demonstrated many times and have seen many poor results because the radiologist was too timid to give the proper dose.

All of you who were at Toronto last year remember that the variation of dose ran from a thousand by one man to about two thousand by another. That shows quite a range of dosage.

There is a special branch of the National Research Council which is investigating the field of radiation. It is anxious to have suggestions by physicians throughout the country for research. It has money to be expended along that line and ample equipment. If you are particularly interested in some special line of research which will help radiation in any form, if you will address any of your remarks to the Chairman of the Committee on Research, National Research Council, Washington, D. C., whether in this year or the following year, the Committee will be only too glad to cooperate with you in any way, and you will also be of great value to it.

Dr. A. L. Gray, Richmond, Va.—I wish to ask Dr. Thrash particularly what his technic was in treating hay-fever.

Dr. J. W. Landham, Atlanta, Ga.—I was very glad to hear Dr. Thrash emphasize the value of radiotherapy in non-malignant conditions. I think that the greatest field of the radiotherapist is in the treatment of non-malignant cases. Radiotherapy has been used in unresolved pneumonia, carbuncles, acne, enlarged thymus, tuberculous adenitis and various dermatological diseases for years, and now it is being used with satisfactory results in many acute inflammatory and pyogenic lesions.

I feel that the field of radiotherapy in non-malignant conditions will continue to expand.

The majority of the cases of malignancy referred to the radiotherapist for treatment are absolutely hopeless regardless of the method of treatment employed. Of course, palliative results are all that can be expected in such cases. Better results are being obtained in carcinoma of the cervix because the patients are being referred in the early stages of the disease.

Dr. Thrash (closing).—The importance of consideration of the mental and physical condition, temperament, the sensitiveness and lack of sensitiveness of the patient to the rays, goes without saying in x-ray therapy. Dr. Coe's point is well taken in reference to approaching the point of tolerance. Only experience enables one to approach the optimum dose intelligently.

For hay-fever, our technic is to shield the eyes and make the exposure without a port. The disadvantage in administering the rays directly in front of the face is that the nose is the nearest point to the focus and this will sometimes suffer. An attempt to screen the nose would naturally screen off some of the sinus areas and would interfere with results. For this reason we treat each side of the face separately, shooting the rays directly upon each lateral sinus. This not only protects the nose and lips, but places the radiation more directly where it is needed. The dosage we use for the accessory sinuses in vascular neuroses, which for a better term we speak of as hay-fever, is 160 kilovolts and 18 inches distance. We use the water-cooled tube and give from 15 to 25 milliamperes and 250 to 400 milliampere minutes usually suffice. This is divided into three treatments given from two to five days apart. We use a filter of one millimeter of aluminum and one-fourth millimeter of copper. Each one of the sinuses should be reached, because in all probability every accessory sinus is involved together with the nasal and pharyngeal mucosa. We have treated only a few of these cases and have gone into the matter carefully and cautiously. We do not know as yet what the outcome will be, but we feel very much encouraged.

We can say the same thing about treatment of the spleen in the case of familial jaundice. What treatment has been used in these cases has not been satisfactory. The technic may have been different from what we have been using. These cases are bad to handle from an operative standpoint, as many of them die. The disturbance is evidently a hyper-splenism, and our object is to reduce this excess of splenic hormone to a more or less normal condition.

The treatment of asthma is certainly one of the chief fields of x-ray therapy. Our experience has been especially gratifying.

Our essay may be considered elementary by the members of this Section, but we are writing for the medical profession generally. We hope that physicians generally may get some insight into what x-ray therapy will do, and that the general profession will cooperate with us in our work.

SYMPATHETIC GANGLIONECTOMY AND RAMISECTOMY FOR CHRONIC INFECTIOUS ARTHRITIS: A CLINICAL INTERPRETATION*

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We present, on invitation, this consideration of the status of sympathetic ganglionectomy and ramisectomy in the treatment of chronic, nonspecific, so-called infectious arthritis with considerable hesitation, because exact analysis of the subject is not as yet possible.

Previous papers have presented in detail the development of the subject. Here we shall review only as much as is necessary for a clear survey of the problem.

PURPOSE AND CIRCULATORY EFFECTS OF THE OPERATION

Sympathetic ganglionectomy and ramisectomy was first applied in cases of spastic paraplegia. The patients, after operation, presented marked and apparently permanent elevation of the cutaneous temperature of the extremities. Adson and Brown instituted the procedure, therefore, in the treatment of certain cases of vascular disease.[1 2 3]

The purpose of the operation is to remove certain sympathetic ganglia and divide their rami, thus to interrupt vasoconstrictor fibers to vessels of the extremities, and to increase circulation, temperature, and possibly metabolism of tissue. Clinical and physiologic studies have demonstrated marked vasodilatation and cutaneous hyperthermia. Vasodilatation seems to occur chiefly in the arteries of moderate size, and in the arterioles. There is probably no vasodilatation of capillaries.

Certain additional changes are produced:[9] complete abolition of reflex sweating in the regions involved, loss of the pilomotor reflex, production of Horner's syndrome after the cervicothoracic operation, and variable reduction of pain. Marked alteration of cardiac rhythm or rate has not been observed. Recent studies by Spurling[57] and Blake seem to demonstrate alterations in cardiac output.

APPLICATION IN THE FIELD OF RHEUMATIC DISEASES

The most efficient and most ancient treatment of chronic rheumatic diseases has consisted in the use of certain physical agents, chiefly heat.

Sympathetic ganglionectomy and ramisectomy seemed to Rowntree and Adson[48] to provide more permanently and efficiently the therapeutic need of constant heat and augmented circulation. But sympathetic ganglionectomy and ramisectomy is by no means applicable to all rheumatic diseases, nor to all types of chronic arthritis.[24] The term "chronic arthritis" needs definition. For various reasons it seemed best to limit the trial use of the operation to two types: (1) that which is a manifestation of a fairly well developed syndrome of scleroderma and Raynaud's disease combined, and (2) that which is most progressive, disabling, and difficult to treat, chronic infectious arthritis. This term is generally synonymous with atrophic, proliferative, rheumatoid, infective, or periarticular arthritis.

The clinical features, localization and progression of the arthritis that accompany scleroderma are generally different from those of chronic infectious (atrophic) arthritis. There is reason to suggest that the arthritis which accompanies scleroderma is one of the results of primary vasospastic disease, and is the articular equivalent of the cutaneous changes; both are due to functional deficiency in blood supply. In these cases, sympathetic ganglionectomy and ramisectomy may be a so-called specific measure. This type of arthritis, as encountered at the Clinic, and the results of sympathetic ganglionectomy and ramisectomy in its treatment, have been described in previous papers.[3 10 37]

In this paper we shall deal only with the part played by a sympathetic ganglionectomy and ramisectomy in chronic infectious arthritis.

SELECTION OF PATIENTS FOR THE OPERATION

Sympathetic ganglionectomy and ramisectomy is not advocated for all phases and degrees of chronic infectious arthritis. The operation, at present at least, does not seem indicated in acute arthritis of any type. Patients with acute arthritis, infectious or not, possess to an indeterminate and sometimes surprising degree the ability to resume function with minimal injury. Neither is the operation applicable in forms of chronic arthritis generally considered to be non-

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infectious, such as the senescent form (degenerative, hypertrophic, osteo-arthritis), the traumatic form, and gout.

The procedure at present is considered only for treatment in cases of chronic infectious arthritis that answer the following specifications:

(1) The patient should be, preferably, less than thirty-five or forty-five years of age. After the age of forty-five years, the presence of arteriosclerosis might prevent adequate vasodilatation, and this would preclude success. Furthermore, although chronic infectious arthritis occasionally originates after the age of forty-five years, the majority of cases of recent duration seen after that age are of other types, chiefly that here called chronic senescent arthritis (degenerative, hypertrophic, osteo-arthritis).

(2) The involvement should be chiefly or wholly in the joints of the hands or feet. Although the cutaneous temperature after operation may increase somewhat over the legs or arms, the increase is greatest in the hands and feet. Elsewhere it may be insignificant and therapeutically inadequate.

(3) The arthritis should be chiefly periarticular or synovial, with little, if any, bony alterations except atrophy. Marked hypertrophy, and especially destruction, are contraindications. Restoration of lost bone and cartilage cannot, of course, be expected. With marked bony changes, similarly, extensive changes in soft tissue and in vascular supply may have occurred, largely with irreparable injury.

(4) The arthritis should have been relentlessly progressive in spite of a period of, probably, at least six to twelve months of intensive treatment by the more established, less radical procedures. If it is not progressive, continuation of treatment already instituted may eventuate successfully.

(5) It would seem of particular importance that the arthritis be associated with abnormal alterations in peripheral and general vasomotor tonus, signified by cold, clammy, sweaty hands and feet, reduction of cutaneous temperature of the fingers and toes below normal, intermittent numbness and tingling, and often reduction of the systolic blood pressure. If the extremities are already warm, resection of sympathetic ganglia and trunks cannot be expected to increase the peripheral circulation, as it is presumed that the caliber of the vessels is already near the maximal degree of vasodilatation.

The exact nature and significance of the circulatory alterations in chronic infectious arthritis are not known. They generally do not occur in other types of arthritis. The time of their apppearance in chronic infectious arthritis is variable. They may occur, as Spender[54 55] pointed out, as one of the earliest manifestations of the disease, or their appearance may be delayed until the later stages. It is believed by some observers that the circulatory changes are of primary significance and play a part in causing the disease of the joints.[14] Others believe, with Garrod, that they are secondary to some generalized toxemia or infection. We are inclined to concur in the latter opinion and believe that the time of their appearance in chronic infectious arthritis, and their presence, depends on the extent and degree to which the sympathetic nervous system is affected by the general toxemia of the disease. Toxins from localized inflammation may be the cause of these vasomotor changes, and may act locally, or perhaps centrally, on a vasoconstrictor center.[7] Thus may be explained not only the vasomotor changes, but also derangements in many systemic functions which do not seem dependent on foci of infection in their respective organs.[23 58]

The cutaneous temperature of normal persons presents a definite gradient in various sites; it is lowest in the distal extremities.[18] Although the cutaneous temperature[61 67] of many patients with chronic infectious arthritis is normal, and in a few cases even above normal, without systemic fever, the average cutaneous temperature, of distal regions at least, is about 4° lower than normal (*Table 1*).

(6) The abnormal vasomotor alterations must be capable of correction, if possible of overcorrection, by means of the operation. Because such specificity as the operation possesses relates almost exclusively to this correction, we shall consider this phase somewhat in detail. The possibility of such correction can be gauged by the response of the oral and cutaneous temperatures to the administration of typhoid vaccine, as is done for the determination of the vasomotor range and index.[29 53]

The increase in cutaneous temperature of normal persons, and of patients with arthritis after injections of vaccine, and of the latter after sympathetic ganglionectomy and ramisectomy, is shown in *Table 1*. After injections of vaccine, the temperature of fingers and toes of patients with arthritis rises about 10° C. (mean). The cutaneous temperatures of the fingers start

Table 1
STUDIES OF CUTANEOUS TEMPERATURE*

Situation	Type of Subject	Temperature at Rest		Temperature After Administration of Typhoid Vaccine		Temperature After Operation	
		Range	Mean	Range	Mean	Range	Mean
Great toe, under surface	Normal	24 to 30	29.2	30 to 38			
	Arthritic	20 to 29	26.1	32.5 to 38	35.3	28 to 36.4	33.3
Index finger	Normal	31 to 33	32.0	34 to 38			
	Arthritic	22 to 32	28.0	34 to 39	37.1	30 to 36.6	34.4

*Temperature is recorded in degrees Centigrade. Studies were made in a special room which was at a temperature of 22 to 26° C.

and end about 3° C. (mean) higher than those of the toes.

The peak of the cutaneous temperature of the extremities after the injection of vaccine in normal persons, and of those arthritic patients studied prior to sympathetic ganglionectomy and ramisectomy is about equal. This indicates that the low cutaneous temperature of patients with uncomplicated arthritis is not due to any organic, occlusive interference with main vessels or with the vessels that supply the skin.

Vaccine seems to produce maximal dilating effects, and the postoperative hyperthermia is about 3° C. less than that of postvaccinal hyperthermia. Thus, after sympathetic ganglionectomy and ramisectomy, the temperature of the fingers has risen about 4 to 8° C. (mean 6.4° C.), and that of the toes 7 to 10° C. (mean 8.2° C.).

It would appear from these figures that in general the degree of rise of postoperative temperature of extremities can be anticipated approximately from the postvaccinal rise. This is of clinical significance in selecting cases, for in our experience, unless patients are assured of a rise of at least 5° C. after operation, improvement will be absent or minimal. To anticipate this there should be a minimal postvaccinal rise of 8 to 9° C.

The estimation of possible vasodilatation has been determined throughout these studies by the vasomotor index of Brown, the estimation of postvaccinal hyperthermia. Since his work other methods have been suggested by White, by Morton and Scott, and by Brill and Lawrence. White, and later Brill and Lawrence, advocated blocking the sympathetic nerves with procaine, affording a temporary postanesthetic rise in cutaneous temperature of exactly the same magnitude as that obtained by sypmpathetic ganglionectomy and ramisectomy.

Factors Influencing Results of the Operation.—Sympathetic ganglionectomy and ramisectomy for arthritis might be viewed either as a non-specific or as a specific form of treatment. As the former, it should be considered that, following operation, the tissues, especially in the periphery, are merely heated, and an attempt is made through a new operation to afford an advanced type of physical therapy by means of increased circulation. Any superiority in results from such an operation may rest solely on the fact that the desired increase in circulation, with attendant phenomena, is maintained over a protracted period of time, possibly permanently, instead of intermittently, as with physical therapy.

With increased circulation and temperature it is hoped that increase of metabolism will occur, and it might be postulated that this increase in tissue metabolism would closely follow van't Hoff's law, namely: that the velocity of chemical reactions is doubled for each increase of 10° C. in temperature. It is hoped the benefits extend to articular as well as cutaneous tissues and that relief of pain also will follow increase in circulation and heat.

If it were permissible to consider the operation a specific procedure, it might be assumed that it is an attempt to arrest an associated neurogenic disturbance either of primary or secondary origin.

Before considering the clinical results of sympathetic ganglionectomy and ramisectomy it is necessary to recall that there are marked anatomic and physiologic differences in the various structures to be affected, such as in the nerve and blood supply of skin and various articular components, and in the regenerative power of the diseased tissues involved. It is only through appreciation of these differences that certain variations in results can be comprehended. Variability in results may be dependent on five points: (1) hyperthermia in tissues of joints may not necessarily parallel that of skin; (2) the blood supply of the different tissues of joints may not be augmented equally, for their vascular supply differs greatly; (3) delivery of blood to

diseased tissues does not guarantee adequate utilization of that blood; (4) pain in arthritis may not be caused by one factor; and (5) there may be new dissemination of infection from hidden foci, or from infected joints not influenced by the operation.

PHYSIOLOGIC CONSIDERATIONS

Relationship Between Skin and Joints.—A definite physiologic relationship exists between skin and joints. Normally, the skin acts as a buffer, and changes in environment are not appreciated by joints, at least symptomatically. In rheumatic patients, however, environmental conditions that affect the skin may proportionately affect the joints, not only through changes in temperature, but also by alterations in barometric pressure and other phenomena of weather. This influence is believed to be exerted through the interaction of the endocrine and autonomic systems, and in arthritis a disturbance in speed of adjustment of the balance is believed to exist.[20 33 44]

Pathologic as well as physiologic relationships exist between the skin and joints of rheumatic persons. The skin may be relatively normal in the early stages of arthritis; later, the vasomotor changes noted produce cold, clammy, sweating skin; still later, the characteristically dry, atrophic, smooth, shiny skin covers the deformed extremities.

Arthropathia psoriatica, the arthritis seen in the combined syndrome of scleroderma and Raynaud's disease, rheumatic peliosis, and erythema nodosum, afford additional argument for definite relationship between pathologic conditions of the skin and the joints. Indeed, in psoriatic arthritis, treatment of the pathologic condition of the skin alone may result in complete remission of the associated disease of the joints.

A diminished blood supply to skin and joints is considered one of the chief features of chronic infectious arthritis.[34 62] Arteriolar constriction is believed by many to exist at its basis. As far as capillaries are concerned, differences of opinion are expressed. Prusik did not find characteristic changes. Pemberton[39 40] has reported that the cutaneous capillaries are constricted, of poor visibility, contain a diminished amount of blood, and that the stream is slowed. The belief has been expressed by Brown that in the majority of cases the capillaries of the nailfold are unaffected, or slightly dilated, and that the stream is slowed. After sympathetic ganglionectomy and ramisectomy, they become not more, but less, dilated, and the rate of flow is increased.[8]

In our studies, the demonstration of augmented circulation after operation was derived mainly, although not wholly, from studies of surface temperature. We realize that an increase in temperature of the skin does not prove that the operation increases temperature within the joint. As Brown has said, temperature of the skin is determined by the status of surface vessels and not of deep vessels. The vascular supply to skin is quite different from that to tissues of joints. The skin is highly vascular and its vessels contain a superabundance of vasomotor fibers. Some of the tissues of joints are of low vascularity, are even avascular. Certain definite differences of temperature may normally exist in relatively contiguous tissues and organs, and the response of adjacent tissues to applications of heat may vary widely.[18] Marked increase in temperature of the skin may be but little appreciated by muscles only a few millimeters away.[60] It is doubted by some that penetration of heat below the skin, even with diathermy, is clinically more than slight.[7]

We must distinguish, however, between raising the temperature of deep tissues by penetration from the surface and by sympathetic ganglionectomy and ramisectomy. It is not expected that hyperthermia of joints results solely from the augmented cutaneous circulation, but, it is hoped, through increased circulation in the articular vessels themselves. Whether variations of temperature of joints after operation are proportional to those of skin is not known, and experiments by Rynearson, Sheard and Craig to determine this are in progress.

Blood Supply of Articular Tissues.—Tissues of joints in the normal condition vary extensively in vascularity, from the highly vascular synovial membrane to the avascular cartilage. The effect of sympathetic ganglionectomy and ramisectomy, then, as far as increased nourishment is concerned, may be different in different regions. The chief source of blood is through the fine network of arterioles which forms the circulus articuli vasculosis of Hunter. The areolar type of synovial membrane, especially the villi, is well supplied with small vessels. The adipose and fibrous types of synovia are less vascular. The cartilages are avascular, except at the extreme periphery, where there are a few vessels. They are supposed to get their nutriment largely from bone spaces or from synovial fluid. The latter at least must afford poor pabu-

lum as compared to blood, at least in its content of oxygen, for the oxygen content of synovial fluid is about equal to that of plasma, or only about a fortieth that of blood. Analysis of synovial fluid from the knees of ten of our patients with chronic infectious arthritis with some hydrops revealed the oxygen content to be from 0.7 to 0 per cent by volume.[43] The normal metabolism of cartilage, therefore, is adjusted to a very low requirement for oxygen.

It is not known how much sympathetic ganglionectomy and ramisectomy will influence circulation of tissues of joints. How far synovial hyperthermia, if it occurs, will influence disease in avascular cartilage is speculative. However, the experimental work of Horton and Craig seems to indicate that definite vasodilatation of deep vessels in the extremities takes place, and the therapeutic success in thrombo-angiitis obliterans and Raynaud's disease would confirm the belief that the vasodilatation is extensive.

In arthritis many data have been reported regarding gross and microscopic pathologic changes in cartilage, bone, and muscles in chronic infectious arthritis,[31] but little is known of the state of the nutrient vessels, the condition of prime importance from the standpoint of this paper. In arthritis and myositis the vascular disturbances are not just functional, as they are believed to be in Raynaud's disease, but are associated with actual organic obstruction to flow of blood in finer vessels. Rosenow[45 46] and Ashby have demonstrated, from microscopic sections of atrophic muscle and thickened articular capsule derived from patients with chronic infectious arthritis, marked thickening, and, not infrequently, complete plugging of blood vessels. The plugging, apparently, was not the result of organized thrombi, but rather of endothelial proliferation. In consequence, the lumens of the vessels, including the arterioles, had become partially or completely obstructed. As a consequence, there result regions of lowered oxygen tension, diminished nutrition, and atrophy. Other observers have demonstrated similar occlusive vascular lesions in acute polyarthritis. Such occlusive lesions, if confined to small and terminal periarticular and articular vessels, would not be sufficient to produce significant changes in the vasomotor index.

Wollenberg believed chronic arthritis to be due to arteriosclerotic vascular occlusion. This theory still has its adherents, although it is now being applied chiefly to hypertrophic (senescent) arthritis and not to chronic infectious arthritis.[21 27 28 59] In Heberden's nodes, considered to be a form of senescent arthritis, the pathologic studies of Brogsitter and of Hench[22] have demonstrated occlusive inflammatory, not arteriosclerotic, lesions, both early and late in the stage of articular change. In rheumatic fever it is, of course, in the study of vascular pathologic changes which, to a large extent, are obliterative, that recent advances have been made.[63]

In chronic infectious arthritis, therefore, as in some cases of thrombo-angiitis obliterans, both vasomotor and occlusive lesions may be present, at least in the finer vessels. Such a condition would modify the effects of operation.

Utilization of an Augmented Circulation by Diseased Tissues.—The ultimate results of sympathetic ganglionectomy and ramisectomy, as of other forms of treatment, must depend on the condition of the diseased cells themselves. The operation will be judged by, and will depend on, the ability of the diseased tissue to receive and respond to augmented circulation. Delivery of blood to diseased tissues does not of itself guarantee utilization of that blood in adequate quantity for healing. If the vascular disturbances are wholly or chiefly functional, early augmentation of the blood supply might readily correct the disturbance, as it does in uncomplicated cases of Raynaud's disease. However, when such disturbances, even if only functional, are of long duration, irreparable cellular injury may occur, which does not respond to correction of the primary functional difficulty. Hence in some cases of chronic infectious arthritis even a marked and permanent increase in the supply of blood to joints at times will be insufficient to correct the inflammatory and destructive components of a well developed pathologic process. The power of regeneration and resolution, furthermore, may not be equal in various structures that are affected in arthritis.

Origin of Pain in Arthritis and Mechanism of Relief.—Little is known of the nerve supply to articular structures. The synovial membrane is well supplied with nerves; according to Fisher, a delicate plexus exists beneath the endothelial layer. These are distinct from pacinian corpuscles, which not infrequently are seen in the actual capsules and ligaments of joints. According to Rost, joint and epiphyseal cartilage is insensitive. The periosteum, of course, is highly sensitive. The compacta is insensitive

to a depth of several millimeters. Nystrom showed that, contrary to earlier views, the marrow cavity is not insensitive throughout.

The pains of chronic infectious arthritis are of several types, and are dependent on several factors. They may be due to inflammatory changes in muscles, tendons, bursae, or various parts of bone; to pressure on enlarged synovial fringes; to stretching of scar tissue; to adhesions; to reflex muscular spasm, and to apposition of articular surfaces covered with sensitive fibrous tissue. Neuralgia of varying anatomic distribution also has been described, for instance, by Jones.

It would hardly be expected, then, that sympathetic ganglionectomy and ramisectomy would uniformly influence the various sites of origin of pain, or would cause immediate amelioration. And yet distinct, at times even complete, relief of pain is an immediate postoperative experience.

It is believed by some, among them Krogh, that there is a definite relationship between the conditions of the blood vessels and sensation.

In the diseases in which trophic changes appear in joints it is the sensory nerves which are believed to be chiefly affected. So little is known, even about undoubted neurogenic arthropathy, that it is not even certain that there are such things as trophic nerves.

Little, if anything, is known of the relationship of joints to the sympathetic nerves. At present, it is extremely difficult[12] to explain the mechanism of sympathetic pain or of relief of pain by sympathetic ganglionectomy and ramisectomy. It has been generally understood that the sympathetic nervous system contains no sensory fibers. But to explain the effect on pain of sympathetic ganglionectomy and ramisectomy, not only in arthritis but in thromboangiitis obliterans and Raynaud's disease, Ranson, Kuntz and others expressed the belief that the sympathetic nervous system contains sensory fibers which have their ganglia in the spinal cord, and that there are sensory fibers associated with the postganglionic fibers which innervate blood vessels. An additional theory is that advanced by Orbeli, namely: that the sympathetic nervous system regulates, in some way, the threshold of pain.

The immediate relief of pain associated with vasoconstriction in Raynaud's disease would suggest that spasm of vessels was in some way responsible for pain. The pain which persists in certain cases of thrombo-angiitis obliterans after sympathetic ganglionectomy and ramisectomy would suggest peripheral neuritis due to changes in tissue about the terminal sensory filaments. In arthritis, the pathologic changes in the articular and periarticular tissues are so varied, probably including changes in the sensory terminal filaments, that one would not expect complete relief of pain in every case following sympathetic ganglionectomy and ramisectomy. Thus, the subject of relief of pain by the operation seems involved at present.

CLINICAL RESULTS OF THE OPERATION

With these various physiologic facts in mind, one can better appreciate the clinical results of sympathetic ganglionectomy and ramisectomy, and it will not be surprising that these results are at times variable and difficult to interpret.

Prior to November, 1930, sympathetic ganglionectomy and ramisectomy was performed at the Clinic for chronic infectious arthritis in thirty-seven cases. In twenty-six instances the lumbar operation was performed; in four instances, the cervicothoracic, and in seven instances, both. No tabular summary can be given at the present time, for the merits of the procedure must be judged by the response of each case. Due consideration must be given for the wide differences in degree of preoperative pain, swelling, stiffness, number and situation of joints involved, duration of illness, extent of incapacity, and response to past treatment.

A note on the preliminary effects of treatment in the first seventeen cases has recently been published by Rowntree, Adson and Hench. The present status of patients treated can be grouped in three classes: (1) those who have obtained definite, in a few instances marked, relief, and whose relief in general has been maintained or progressive; (2) those who have obtained definite, at times even complete, relief of pain, and to a less degree relief of other manifestations, but who have had partial or complete relapses, and (3) those who have obtained little, if any, postoperative or subsequent relief.

Several patients were accepted for operation only because they presented desperate conditions and the operation seemed justified. Several did not wholly conform to the criteria by which patients are generally selected. All the patients had become discouraged, some because of long years of therapeutic trials. The average duration of arthritis was five and a half years;

the maximal duration, eighteen years; the minimal duration, four months.*

Considering these facts in the light of our experience, as well as in the light of the experience of Flothow[16] [17] and of Spurling,[56] it would seem that in general the early postoperative effects have been satisfactory.

A review of the preliminary effects of the operation has shown, however, the diversity of results that one might expect with the foregoing physiologic and pathologic considerations in mind. It has demonstrated that it is difficult to predict the exact outcome in a given case. In one case in which a good result might have been anticipated, little relief was obtained. In another, in which the operation was performed with remote possibilities of relief, definite benefits were derived (*Table 2*). In one instance

Table 2
RELATION OF POSTOPERATIVE HYPERTHERMIA TO IMPROVEMENT IN CONDITION OF JOINTS

Case	Type of changes disclosed roentgenographically	Preoperative temperature of great toe, degrees C.	Postoperative rise of temp. of great toe, degrees C.	Relief	
				Grade	Permanence
17	Periarticular	24.1	10.0	2 to 3	Maintained
11	Periarticular	24.1	10.0	2 to 3	Not maintain'd
3	Periarticular	24.7	3.7	2 to 3	
12	Periarticular	23.0	10.8	2 to 3	
7	Periarticular	28.0	6.1	*	
6	Periarticular		10.4	1	Slow imp'vm't
13	Destructive		8.0	3	Maintained

*No definite relief.

marked increase of cutaneous temperature was associated with disappointingly little improvement; in another, with only a moderate rise of cutaneous temperature, surprisingly definite relief was afforded. In one instance, with only periarticular disturbances present, which were limited to the feet, benefits were slow in appearing; in another, postoperative relief of pain was surprisingly great in spite of polyarticular destructive changes.

*This patient was admitted for operation because of marked progression within four months and inability to stand the prolonged expense of medical care. Occasional exceptions seem justified for economic reasons.

Relation of Postoperative Cutaneous Hyperthermia to General Improvement of Joints.—Undoubtedly the best results are obtained in the hands and feet, regions in which postoperative temperature is greatest, in contrast to more proximal joints, where the increase in temperature is much less marked. Therefore, one might expect general correlation between increased cutaneous temperature and decreased inflammation. Within certain limits it is true that beneficial results in joints are proportionate to the increase noted in the temperature of the overlying skin. Yet no perfect parallelism nor absolute consistency in the relationship can be demonstrated.

It is not surprising to note the absence of consistent correlation between cutaneous hyperthermia and improvement in the joints. Many patients who have arthritis are not relieved by protracted heat, even by prolonged exposure in the tropics. Observers are unable to find absolute parallelism between the relief obtained and the amount of fever produced by foreign protein. Individual variations in any physiologic reaction and pathologic process may alter the results. Other things being equal, however, experience would seem to indicate that the results obtained by these different measures in general parallel the degree of hyperthermia.

Postoperative Relief of Pain.—Pain as a symptom of chronic infectious arthritis is so bound up with other phenomena of the disease, such as swelling, redness and stiffness, that the results in relief of pain hardly can be analyzed separately. Reduction of swelling, redness, and stiffness may lag considerably behind reduction of pain. Relief of pain is often dramatic in its immediate postoperative appearance. Sometimes it is complete in all joints of the extremities involved in the operative field. At other times, relief of pain is confined to distal joints, where increase in temperature is greatest. Sometimes amelioration of pain is continued after resumption of activity. At other times relief is incompletely maintained, and pain may return when the patient becomes actively ambulatory. In general, it seems that relief of pain has appeared most promptly in these cases in which the greater increases of hyperthermia of the skin have occurred.

Frequently, following lumbar sympathetic ganglionectomy and ramisectomy, striking relief of pain may be noted in joints of the upper extremities, which have not been released from sympathetic control. This, however, lasts only

a few days, and probably is dependent on the vasodilating effect of the general anesthetic, on the metabolic stimulation from the shock of the operation and on rest in bed.

Relation of Effects on Skin and Joints.—We have considered, briefly, some physiologic and pathologic relationships between skin and joints in rheumatic diseases. Although they may be associated in disease, this association may not be evident in their response to treatment. The response of the skin to sympathetic ganglionectomy and ramisectomy may not be analogous to that of the joints, however, and vice versa. For example, in *Case 17* there was chronic arthritis (probably arthropathia psoriatica) in association with psoriasis of the nails and skin. After operation there was definite improvement in the arthritis of the extremities, but the psoriatic condition of the nails remained unchanged. In *Case 29*, chronic infectious arthritis was associated with mild Raynaud's disease and mild scleroderma, the latter probably of a secondary type. Ganglionectomy and ramisectomy improved the condition of the skin markedly, but five months after operation there was little, if any, improvement in the arthritis.

Laboratory Studies.—Craig and Kernohan have been conducting microscopic studies of the removed sympathetic ganglia, which do not reveal constant pathologic change denoting a local reaction. This would seem to confirm the belief that the alterations in the sympathetic nervous system are central in origin and secondary in character.

Considering the differences in blood supply to various parts of joints, and the varying potentialities of joints (bone, cartilage, synovia) to regenerate, it is not expected that gross loss of bone and cartilage will be materially altered. The only roentgenologic change that might be anticipated within the space of a few months might be diminutive of atrophy of bone. Our roentgenologic studies are incomplete, and to date marked postoperative differences have not been noted.

Whelan and Hench have made certain chemical studies to determine, if possible, whether, after sympathetic ganglionectomy and ramisectomy, there were chemical evidences of increased oxidation. The postoperative changes appeared to be of little significance and definite conclusions could not be drawn from the results. The studies are being continued, however.

CARE SUPPLEMENTARY TO OPERATION

Following sympathetic ganglionectomy and ramisectomy for chronic infectious arthritis, the postoperative complications have not been particularly serious, and in this entire series of cases there have been no deaths.

Adson and Rowntree have emphasized the need for considerable restriction in motion of joints, and particularly of weight bearing, after operation. With reduction of pain, the tendency of the patient is to overactivity. Certain supplementary measures may be necessary also, and general measures should be used to improve the patient's general condition. The numerous procedures that are believed to have effect in raising specific and non-specific immunity, and which are already utilized in the treatment of arthritis, should be resumed. These are corrective diets, administration of specific and non-specific vaccines and serums, and removal of foci. Efforts must be made to prevent reinfection from disregarded foci or from infected joints uninfluenced by operation.

CONCLUSION

Sympathetic ganglionectomy and ramisectomy in the treatment of chronic infectious arthritis is not an end in itself, but a means to an end. It is a procedure of variable potency, the ultimate success of which probably will depend in each case on the ability of the cells of articular tissues to receive and respond to the augmented circulation provided thereby.

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DISCUSSION (*Abstract*)

Dr. Alfred W. Adson, Rochester, Minn.—Sympathectomy is not a cure-all for arthritis, nor is it indicated in infectious or senescent arthritis. It is only indicated for a small group of patients, who have failed to respond to the usual forms of treatment. It proves of value in cases when arthritis has affected the peripheral joints such as the fingers, hands, wrists, toes, feet and ankles, when it is apparently due to a vasomotor disturbance characterized by cold, clammy skin, and when it is temporarily relieved by some form of heat. The object of sympathetic ganglionectomy and trunk resection is to interrupt all vasomotor nerves to the arteries supplying the areas involved in order to prevent vasoconstriction and to accomplish permanent and continuous dilatation, thus producing a marked increase in blood flow which naturally warms the extremity and which increases oxidation and elimination. By measurements of the retinal arteries before and after cervicothoracic ganglionectomy, Dr. Wagener of the Section on Ophthalmology of The Mayo Clinic has shown that the arteries and veins are dilated from a third to half the size they were previous to sympathectomy and that this dilatation has remained permanent, all of which substantiates the argument that the circulation to the affected extremities is materially improved. The results in the treatment of the small arthritic group have been satisfactory, but the treatment has offered no relief in the presence of ankylosis except for pain. Little relief has been obtained in the treatment of the larger joints, such as elbows, shoulders, knees and hips, and sympathectomy would not be advocated if these joints were alone involved.

Dr. H. Theo. Simon, New Orleans, La.—The chemical constituents of the blood also have some influence on the smooth muscles, so that the artery will not dilate and disintegrate. Dissecting the sympathetic fibers also removes the central influence, if you take all of them.

None of these patients has been incapacitated because of cardiac insufficiency. We have had them climb stairs.

Dr. Hench asked me to discuss the question of pain. Dr. Koontz and Dr. Ranson believe that pain fibers return with the sympathetic fibers, and if you section them, you have completely diminished the pain stimulant.

It is possible that the improvement in the metabolism plays a role, just as a cramp in the leg is relieved by the application of heat.

CHAGAS' DISEASE IN PANAMA: REPORT OF THREE CASES*

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More than two decades have elapsed since Chagas' disease, or American trypanosomiasis in the human being, was first discovered in Brazil by Dr. Carlos Chagas[1] (1907) and later (1909) reported by him. Since that date, a few cases of what appeared to be the same disease have been reported from time to time in other parts of the Western Hemisphere. This may indicate either a slow spread of the disease or a better knowledge of the clinical manifestations and greater use of the laboratory as an aid in diagnosis. It is likely that the geographical extent of the disease is much greater than has been previously suspected, since it is found usually in children and the period of time that parasites can be demonstrated in peripheral blood films is relatively short, thus making a diagnosis by this means largely a matter of chance.

Geographical Distribution.[2]—Cases have been recorded in Brazil (provinces of Minas Geraes, Sao Paulo and Goyaz), in Venezuela (states of Trujillo and Miranda), in Argentine (Tucumen and Jujuy), in Peru and in Salvador.

Trypanosoma cruzi, or trypanosomes resembling it, have been found in bugs (*Triatoma* and *Rhodnius*) in the Argentine and in California, but they are said not to transmit the disease to man in these regions.

Robertson[3] reports *T. cruzi* (1929) in an opossum captured near Tela, Honduras, C. A. It seems strange, with cases reported both below and above Panama, that no cases have been previously discovered in Panama or the Canal Zone, particularly in view of the fact that vast numbers of routine blood film examinations have been made in the hospital, dispensary and field services. The first case reported here is from the service of Dr. Rodolfo Arce, of the Hospital Santo Tomas. It was discovered purely by chance in the routine examination of blood films for malaria. The other two cases were discovered by the Gorgas Memorial Laboratory while conducting a blood film survey for ma-

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laria in the basin of the Chagres River. All of these cases came from the village of Aguas Buenas or its immediate neighborhood. This village is located on the new Madden Dam Road near the Canal Zone boundary. The first patient lived about two miles from the village and about 50 yards from the Madden Dam Road. The other cases are members of a family that lives in Aguas Buenas. The homes of the patients are of the typical rural native type, consisting of palm leaf roofs and cane walls with a dirt floor, the sleeping quarters being in the attic of the house on split bamboo or board ceiling.

Case 1 (Hospital Santo Tomas Case 111463).—E. B., a female infant of Panaman parents, aged 18 months, was born in San Francisco de la Montana, near Santiago de Veraguas, and had lived for the previous two months on the Madden Dam Road near Aguas Buenas. She was admitted to the Hospital Santo Tomas November 28, 1930, with a diagnosis of acute gastroenteritis. The history of the illness could not be obtained, as no member of the family has visited the hospital since the child was admitted. The child was poorly nourished and poorly developed. The facial expression was dull and mask-like. The scalp was covered with a lot of dirty gray crusts and numerous pustules. The skin of the entire body was covered with scars, apparently the result of old insect bites. The eyes were normal. The thyroid gland showed no evidence of enlargement. The posterior cervical glands were large and hard and were somewhat more enlarged on the left side than the right. The left axillary and both inguinal sets of glands were palpable, but not so large as the cervical sets. The heart and lungs were normal. The abdomen was distended, pendulous and thin walled. A small umbilical hernia was noted. The spleen could not be palpated.

The temperature on admission to the hospital was 100° and it has since remained between 96.4° and 98.8°.

The pulse was 120 on admission and has remained between 100 and 130.

The respiratory rate has remained between 20 and 30.

Electro-cardiographic examinations showed no variation from the normal.

Laboratory Examinations.—Carlos de Seda, of the Santo Tomas Hospital Laboratory, while examining a thick blood film of the child on December 1, 1930, found eight trypanosomes. These parasites varied in number in the blood films, but reached a maximum of 296 per thick blood film on the thirteenth day after admission and then gradually diminished in number until they disappeared from the peripheral blood films on the twenty-eighth day after admission. The films for the past three months have remained negative for trypanosomes.

BLOOD COUNT

Hemoglobin 30 per cent
Red blood cells 1,600,000
Color index 0.93
Leucocytes 9,000
Polymorphonuclears 58 per cent
Small lymphocytes 20 per cent
Large lymphocytes 3 per cent
Large mononuclears 7 per cent
Eosinophils 12 per cent

One estivo-autumnal gamete parasite was found.

The blood Wassermann test was negative.

A slight trace of albumin was the only variation from the normal that was found in the urine.

There was a heavy infestation of the stool with *Ascaris lumbricoides* and a light one with *Trichocephalus trichiurus*.

Treatment.—No specific treatment directed at the trypanosomiasis. After a vigorous treatment for the intestinal parasites the patient showed a steady general improvement.

Case 2 (Hospital Santo Tomas Case 115922).—T. R., a female child of Panaman parents, aged 2 years, was born at Aguas Buenas and has lived there continuously except for the second six months period of her life, which she had passed in the city of Panama. This patient was admitted to the service of Dr. Jose M. Nunez in the Hospital Santo Tomas on March 9, 1931, with the diagnosis of Chagas' disease.

The past history was negative except for the record of occasional attacks of fever and the passage of worms in the feces.

Physical Examination.—The child was well developed and nourished. Its facial expression was bright.

Numerous scars, apparently from old insect bites, were found on the arms and legs.

The thyroid gland was normal.

The axillary and inguinal lymph nodes were slightly enlarged.

There was a slight clear discharge from the eyes and nose.

The lungs were normal.

The heart rate was 120 and slightly irregular. A systolic blow was recorded. The abdomen was pendulous and soft. There were no masses. The spleen was non-palpable. The temperature ran a normal course with a range of 97.2 to 99°. The pulse averaged 100. The respiratory rate averaged 24. There were no physical signs of disease other than those shown by laboratory findings.

Electro-cardiographic examination was normal.

Laboratory Examinations.—Joseph J. Romanchek, of the Gorgas Memorial Laboratory, found a trypanosome in the blood film taken from this child on March 3, 1931. Since that date one or two have been found in routine hospital examinations.

BLOOD COUNT

Hemoglobin 65 per cent
Red blood cells 4,330,000
Leucocytes 9,200
Polymorphonuclears 67 per cent
Small lymphocytes 23 per cent
Large mononuclears 5 per cent
Transitionals 3 per cent
Eosinophils 2 per cent

No malaria parasites were found.

The urine was normal.

The stool was positive for *Ascaris lumbricoides*, *Strongyloides stercoralis* and *Trichocephalus trichiurus*. Light infections were indicated.

Treatment.—No specific treatment for trypanosomiasis was instituted.

Case 3 (Hospital Santo Tomas Case 115923).—J. R., a male infant of Panaman parents, aged 6 months, was a brother to the second case. He was admitted to the service of Dr. Jose M. Nunez at the Hospital Santo Tomas on March 9, 1931, with the diagnosis of Chagas' disease.

The past history was negative except for attacks of fever and the history of passing worms in its stools. *T. cruzi* was found in blood film during a malaria survey by Joseph J. Romanchek. This child was born in Aguas Beunas and has lived there continuously.

Physical Examination.—The child was well developed and nourished. Its facial expression was normal.

There were many scars over the body and extremities suggestive of old insect bites.

The thyroid gland was normal.

The right cervical lymph nodes and the inguinal lymph nodes were moderately enlarged.

There was a slight discharge from the eyes and nose and a cough of mild degree.

The heart was normal.

The abdomen was pendulous, soft, and contained no masses.

The spleen was non-palpable.

The temperature was 96.4 to 99°.

The pulse was 90 to 120 per minute.

The respiratory rate was 22 to 30 per minute.

Electro-cardiographic examination was normal. There were no physical signs of serious illness.

Laboratory Examinations.—Since admission to the hospital the blood films have shown one or two trypanosomes in each thick film.

BLOOD COUNT

Hemoglobin 60 per cent
Red blood cells 3,820,000
Leucocytes 8,200
Polymorphonuclears 65 per cent
Small lymphocytes 27 per cent
Large mononuclears 4 per cent
Transitionals 2 per cent
Eosinophils 2 per cent
No malaria parasites were found.
The urine was normal.
In the stool many ova *of Ascaris lumbricoides* were found.

Treatment.—No specific treatment for trypanosomiasis was given.

Morphology of the Trypanosome.—The trypanosomes found in the blood films of all three cases were morphologically similar to *T. cruzi*, and tissue sections of the heart muscle in an animal infected with the parasite showed a typical localization of leishmania forms.

A detailed report will be made at a later date by the staff of the Gorgas Memorial Laboratory, where research work is in progress regarding an entomological survey of the local area where these cases were found, as well as a study of the disease in wild and domestic animals.

SUMMARY

(1) Three cases of Chagas' disease are reported, found for the first time in the Republic of Panama. All came from one focus in the basin of the Chagres River.

(2) The trypanosomes found in the three cases are believed to be *T. cruzi*.

(3) The trypanosomes disappeared spontaneously from the peripheral blood films without the action of any specific drug in the course of a few weeks. No opinion will be ventured regarding the final outcome of the attacks in these three children.

(4) The symptoms and physical signs of Chagas' disease presented by these cases were essentially negative.

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A STATE-WIDE DENTAL PROGRAM*

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A consideration of public health must of necessity include all the agencies concerned in it. No one phase of health can be neglected without impairing the completeness of the public health organization.

Virginia, early in her public health activities, recognized the need of dental representation on its advisory health board, and in 1916 the law was amended to include a dentist as a member of the Board of Health.

The several steps leading up to our present Mouth Hygiene Division of the Bureau of Child Health may be briefly summarized as follows:

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LEGISLATIVE ENACTMENT

The West law, passed by the Legislature in 1918, provided for the training of our public school teachers so that they might be prepared to make a physical inspection of school children at least once a year. This inspection, which of necessity was very superficial, including only such inspection as the teacher could make of the vision, hearing, weight, evidence of mouth breathing (indicating adenoids and diseased tonsils), and the teeth, revealed startling physical defects.

COOPERATION OF DENTAL PROFESSION

The percentage of dental defects was so large and the number of dentists located in the rural sections of the State so small that it was decided that the Virginia State Dental Association be informed of the existing conditions and requested to make recommendations as to the best method of meeting them.

This was done, and as a result a former president of this Association was employed by the State Board of Health to make a survey of the State and to recommend to the Board and Association such action as he deemed necessary. His recommendation was that some form of corrective dental clinics was necessary and that they should be carried on by the State Board of Health. As a result of this recommendation, a Director of Mouth Hygiene was appointed and reported for duty on April 15, 1921.

THE VIRGINIA PLAN

It is unnecessary to go into the various plans tried out during the first few months, but we shall give you the results of the experiments which have proved so satisfactory with us that practically no changes have been made in our methods since March 1, 1922, when the present plan was put into operation.

(1) We started with the assumption that the best results could be obtained by cooperation between the State Board of Health, the county authorities and the children. It was definitely decided that the parents should be required to contribute towards the cost of the clinic in proportion to the number of dental treatments found necessary. This contribution we fixed at fifty cents per treatment, therefore a child needing a dental prophylaxis (cleaning), one extraction and two fillings, four treatments in all, would be required to contribute the sum of two dollars. This was not intended to exclude those children whose parents were unable to contribute this small sum, and we never refuse to do all of the dental treatments necessary for such children which can be undertaken at the clinic. The aggregate contributions by the children have averaged approximately $110.00 less than the total cost of each clinic each month, and this deficit is cared for by the State and county, each paying one-half. Or more concretely expressed, the cost to the State is approximately $55.00 per month, or $500.00 per school term of nine months, for each clinician employed.

(2) After trying out various means of employment of dental clinicians, such as by the hour, day, week and month, it was decided to use only full-time clinicians employed for the school term. This was in keeping with the fixed policy of the State Department of Health to use full-time employees only.

(3) Where there is a health officer in the county the clinic is placed under his direction as an integral part of the county health work.

(4) Treatment is limited to oral prophylaxis, amalgam, cement and in selected cases porcelain fillings and necessary extractions. No gold fillings, crown and bridge restorations or treatment of pulpless teeth are undertaken. If root canal treatment is thought indicated and there is reason to believe that the parent would have this done by the family dentist, we urge that such treatment be had immediately. On the other hand, if there is reason to believe that this treatment cannot, or will not be secured by the parent, extraction is immediately resorted to to remove a source of potential focal infection and of possible continuous or periodic suffering on the part of the child.

(5) In conformity with the opinion of the best authorities, we insist that the first or deciduous teeth receive the same care as the second or permanent set.

(6) We hold our clinics for white children and for colored children separately.

(7) We treat the children in the first seven grades only. A careful examination of the mouths of the high school pupils is made and a chart of the defects found is sent to the parents urging that the necessary treatments be undertaken.

FIVE POINT PROGRAM

As a result of efforts to secure the corrections of the physical defects found by the teachers a movement known as the Five Point Program was instituted. This provides that where a child is found by the teacher to have apparently normal

vision, hearing, teeth and throat and is not more than 10 per cent under nor 20 per cent overweight, he or she receives a certificate signed by the State Health Commissioner and the State Superintendent of Public Instruction and stamped with a seal of these two departments stating that this child has met the minimum requirements of the Five Point Program.

It is surprising how much interest is taken not only by the children but by their parents in an effort to secure the corrections of the defects found by the teachers. It must be distinctly understood that while the Five Point Program is purely a teachers' project, still an effort is made to have the throats examined by a physician and the teeth examined by a dentist.

Reports from dentists all over the State show that thousands of children are voluntarily visiting dentists and other thousands are transported by the teachers in school buses to have the necessary dental defects corrected. While we know that in certain sections of the State, where it is impossible for an examination of the teeth to be made by a dentist, some children with dental defects are receiving the Five Point Certificate, still we are satisfied that this program has been the means of securing dental corrections to an untold extent.

In our estimation this has been one of the greatest movements ever started to promote health among the school children. The movement is growing year by year and our hope is that some time in the future all the children in the public schools of Virginia will receive an annual examination by a dentist.

A REMARKABLE DEMONSTRATION

One of the most remarkable health projects ever carried on by any county or state was instituted in Southampton County, Virginia, last year under the direction of Dr. B. B. Bagby, County Health Officer. When a dental clinic was arranged for this County Dr. Bagby stated that his hope was that he could have a 100 per cent correction of all dental defects of white children. This was a colossal undertaking due to the fact that Southampton County had at that time only three dentists, who were all located in one town on the extreme eastern border. Another dentist afterwards located in the County near the southern border. A careful examination of the mouths of children made with an explorer and a mirror showed that, of the total enrollment of 1,991, 1,666 children had a total of 4,682 dental defects. In an effort to interest the parents to correct these defects a letter, signed jointly by the Superintendent of Schools and the County Health Officer, was sent to the parents of every child in the schools, stressing the importance of the care of the teeth and asking cooperation in having the defects corrected. As a further inducement, a half-day holiday was promised to each class room when all of the dental defects in that room were corrected and an extra day holiday to each school when all of the defects in that school were corrected.

The Health Officer realized the necessity of securing a 100 per cent cooperation on the part of the teachers and an extra day holiday was promised at Easter if the entire County went over the top. As a result of all of the publicity and work on the part of the health and school authorities, two days before the Easter holiday began the Health Officer had in hand, either from the school clinicians or the private practitioners, certificates that they had either corrected all dental defects or had collected the necessary sum of money to pay the cost of all defects to be corrected.

There was one little hitch on the last day in one school where one boy who had recently moved into the County needed to have two deciduous teeth extracted. He did not seem willing to part with these two offending members, and, although the County Superintendent, Health Officer, nurse, the dentist and even the preacher visited the mother, she would not agree to have the teeth removed until the spirit moved the youngster. Upon hearing the decision, some of the boy's classmates invited him out to the woodshed and offered to assist in the removal of these two teeth. Thinking that possibly the dentist could remove them better than his classmates, he agreed to go to the clinician and have the teeth extracted, thus making the white children of the County 100 per cent dentally correct. All of the treatments paid for before Easter were actually performed before the end of the school term, thus making the white school children of Southampton County, Virginia, as far as we know, the first and only county in Virginia, or any other state, to be 100 per cent dentally fit.

CLINICS AND PRIVATE PRACTITIONERS

Now, as to the economic value of this demonstration from a purely dental viewpoint. Of the 1,666 children needing dental treatment, 904 children were actually treated by the school dental clinician and 762 children were treated by

the dentists in Southampton and adjoining counties. One of the county dentists who charges average fees estimated that if all of the children treated by the private practitioners had the same number of defects as those treated by himself and if the other dentists charged the same fees, the clinic was the means of sending to the private practitioners more than $5,000 in additional fees during the six months which it lasted.

The writer has on numbers of occasions been approached by private practitioners in counties where clinics have been formerly held with the inquiry as to when the next clinic will be conducted. These practitioners always state that the dental clinic is a great stimulus to their practice not only in sending school children to their office, but is a means of educating the parents to the necessity of dental treatment.

The following is a summary of the activities of the Mouth Hygiene Division of the Bureau of Child Health, State Department of Health, for the past nine years:

Number of counties in which clinics were held	78
(There are 100 counties in Virginia)	
Number of clinics held (each school term during which clinician worked counted as a separate clinic)	236
Number of children examined	225,092
Number of children treated	112,446
Total number of operations	350,148
Total cost of clinics	$226,482.49
Total contributed by children	$131,353.50
Net cost of clinics	$ 95,128.99
Number of full-time clinicians employed	46
Number of part-time clinicians employed	40
Total number of clinicians	86

While the contribution of fifty cents per operation is small, the aggregate contributions by the school children take care of approximately two-thirds of the entire cost of the clinic. If it were not for these contributions we could take care of only one-half of the counties now receiving this service. It might be added that the largest dental dispensaries in the country with unlimited endowment make it a rule that every child treated must contribute a small sum for each treatment.

DISCUSSION (*Abstract*)

Dr. John Collinson, Baltimore, Md.—Maryland's program, inaugurated late in 1929, has the opportunity to profit by the experience of other states. One of the first offcial acts of the Chief of the Division of Oral Hygiene in Maryland was to visit and see first-hand the work as carried on in our neighboring state, Virginia.

Other states were written requesting outlines of their dental programs. In this way it was determined that, largely, three methods were being employed: first, educational programs in which all efforts are directed toward making lay people, teachers, public health workers and dentists "children's dentistry conscious." Corrective work is expected to be accomplished at the hands of practising dentists through the creation of a demand for it. No school clinics are organized or sponsored.

A second plan endorses the establishment of school dental clinics as the most vital factor. Correction of existing defects, particularly in the mouths of poorer children, is stressed. Educational phases of the work are not emphasized except so far as they are the by-product of the clinical work.

The third plan, and the one by which Maryland may be classified, combines the first two plans. Clinics are established and conducted similarly to Dr. Ballou's plan. When possible, and because the magnitude of the problem necessitates such an attitude, the clinical work is limited to the children of the lower grades, preferably to the first three grades. This permits more preventive work as differentiated from correctional treatment.

When possible, Virginia's plan of clinics has been followed exactly. But while Maryland has only recently inaugurated a state-wide program, there had been many community programs started as local clinics previous to 1929. Most of these differ one from another in details of clinic administration. Many did not coincide with the intended State plan. But it was not considered wise nor necessary to revolutionize these clinics and install an absolutely arbitrary method of conduct. Rather these clinics have been aided, financially and otherwise, by the State's Division of Oral Hygiene despite the plans pursued by the clinic. In some, suggested changes more nearly conforming to the State's ideas have been accepted.

Nor has it been found feasible to hold to an exact plan in the inauguration of new clinics. Though Maryland is a small state of only twenty-three counties, varied conditions and attitudes exist. It has been felt better to abide by a local situation rather than inhibit a program's progress by insisting on certain exactitudes.

Aside from the educational value of the clinical or corrective work, there are three phases to the educational phase of Maryland's program.

(1) *Lay Education.*—By means of pamphlets, films, talks, books, it is hoped that the reasons behind the value of mouth health may be brought to lay people, children and adults both. This campaign stresses three main factors in oral hygiene: diet, early and regular dental care, and cleanliness.

(2) *Teachers.*—Believing the best individuals for teaching oral hygiene are the school teachers, rudimentary courses in the subject will be introduced into all of the State normal schools.

(3) *Dentists.*—One of the hardest problems of all mouth hygiene work is to get practising dentists to do children's work. The rank and file of dentists dislike and avoid working on children. Maryland does not hope to convert all her dentists, though some have shown a changed attitude since the State's program inception. By including a course in children's dentistry in the curriculum of the Baltimore College of Dental

Surgery, it is hoped that new graduates may assume an interested attitude toward preventive dentistry in children.

Dr. Jas. A. Hayne, Columbia, S. C.—We have in South Carolina a whole-time Dental Commission whose duty it is to supervise dental clinics held over the State. We started with a 50 cents charge, but we soon found it was not a good idea, and so we do not charge anything. We have about eleven whole-time dentists who are at work in the counties. This year we have a new appropriation, tied in with the Department of Education. We have a law in South Carolina whereby the State pays for six months of the school teachers' salaries and the county pays either one or three months to make out the nine months. That is a very large sum of money. We have about 400,000 children in the State and it takes a good deal of money to teach them. The sum is not budgeted with the closeness and care that other sums are budgeted and every one gets a slice out of the large sum of money. We tied on to it this year and got the Board of Education to agree to give us $600.00 to establish the teaching of oral hygiene, that is, it is going to be a kind of teaching demonstration. The teachers are not only going to teach but demonstrate. We got $600.00 from the Board of Education to work on.

Dentists are more practical than doctors. Dentists are aware of the fact that these demonstrations are going to send them patients, and these children are going to be patients for the balance of their lives as a result. Doctors do not seem to see the demonstration as a means of bringing money into their pockets. We all know that when we started the demonstration of tonsils and adenoids it was a very rare thing after the demonstration if the child needing a tonsillectomy, or the child with adenoids did not seek an operation. In any medical audience the well-dressed, the well-appearing men of the audience are ear, nose and throat men.

Dr. H. S. Mustard, Nashville, Tenn.—The question here seems to be between the Virginia plan, where fees are charged, and the South Carolina plan, where there is no charge. I was born in South Carolina and have worked in Virginia. Therefore, our Tennessee plan ought to contain elements from both of those states. In Tennessee we have, in general, followed Dr. Ballou's program. First, we approached the State Dental Association, which appointed an advisory committee. Inquiries were then addressed to every state in the Union in an effort to learn the details of the various public health dental programs in this country. The results of our investigations were submitted to the advisory committee of the State Dental Association and the Virginia plan was adopted with some little modification.

We quite agree with Dr. Ballou that it is good policy to have the child pay something for the dental service he receives, though we must confess that in some of the counties in Tennessee very few fees have been collected: markedly lower than in Virginia.

We have insisted upon the participation of the local dentists in the program. We have laid down as a fundamental that the criterion of the success of the dental work will not be the number of children served by our dental clinicians, but rather the increasing number of younger children going regularly to their own dentists. It will require a few years for the soundness of our program to be determined. Certainly, we do not expect to serve the dental needs of the children of the State by a staff of dentists. Rather we hope to drive home the desirability of regular dental observation and care by the resident dentists of each community.

Dr. Allen F. Murphy, Beckley, West Va.—I have this difficulty, as I presume every other county health department has, of trying to get the deciduous teeth removed when they are decayed. Many children have returned stating that their dentist advised that the deciduous teeth should not be removed regardless of how badly they were decayed. They are sent back with defects not corrected. Having no dental department, we have not been able to solve the problem of the removal of decayed deciduous teeth.

Dr. Ballou (closing).—We have a great deal of trouble in getting some practitioners to agree over first or deciduous teeth, but we require that when a child goes to a local dentist to have his defects corrected, the dentist must sign a certificate that he has done certain work for the child: cleaned the teeth; removed all roots or abscessed teeth which cannot be successfully treated; filled all cavities in both the first and second sets of teeth which in his opinion could be successfully filled; treated with silver nitrate all teeth which cannot be filled and which will probably be lost within six months from date. Some dentists will sign certificates that they have performed all the operations they think necessary without specifying detailed operations. We always accept such certificates because we want cooperation. When cases of this kind are reported to us we try to write to all the dentists in that immediate neighborhood, so that one man will not think he is being singled out, calling attention to the failure of some dentists to meet our standards and requesting their cooperation.

We regret that we have not sufficient money in Virginia to carry on a program by which we could treat all deserving cases free. We do not believe in free dental service, and in support of our practice I would like to report what our colored clinician stated at a meeting of the State Negro Dental Association which I attended. When we mentioned that the children who are financially able are required to contribute, one of the members got up and stated that in his opinion children should get free education, free text books, free medical and dental service, and practically free everything on earth. Our clinician, who was raised in Mississippi, replied: "The trouble with the negro today is that he has been pauperized too much. Give him anything today, tomorrow he will expect it and if he does not receive it he will demand it as his right." This can be applied with equal force to certain white people.

As was stated, the Eastman Dental Infirmary at Rochester requires the children to pay a small sum every time they visit the clinic. We think the child will appreciate this service more if he has to pay something, however small the amount may be. Our experience proves this to be true. In one of our lower counties one year when cotton was selling low, the children went out and picked cotton and used the money thus earned to pay for having their dental work done. The parents could not understand why the children worked so hard. When they found out they were paying for their own dental work they told us they would see that the children thereafter took care of their teeth.

Our procedure is educational as well as corrective. The teacher makes daily inspection to check up on the care of teeth. A great many keep a daily tooth brush

chart and enter on it the name of the child and whether or not he cleaned his teeth that day. We are finding out just this: all children treated, some in clinics, others by family dentists, take increased interest in their teeth. The five point certificate lasts only one year and must be checked up each year.

THE SIGNIFICANCE OF TYPHOID AGGLUTININS IN THE SERUM OF NORMAL PERSONS*

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The Widal reaction, one of the first laboratory aids proposed in the diagnosis of disease, still holds, after almost 35 years, an important place among diagnostic tests. Considerable dependence is placed on it, in spite of increasing experience with the pitfalls which attend the interpretation of results. It is common knowledge that increasing use of typhoid vaccine has diminished the value of the test. Evidence is also accumulating that other causes than typhoid fever or typhoid vaccination may stimulate the production of typhoid agglutinins,[1] but data regarding the frequency of their occurrence in the general population are scanty.

Rosher and Fielden,[2] in 1922, examined 1,000 specimens of serum and found that 29 per cent were positive. There was a great disparity of sex: 42 per cent of males and only 5 per cent of females gave a positive reaction. These results were attributed to the effect of wholesale vaccination of army men during the World War. This explanation is strengthened by the findings of Smith, MacVie and Newbold,[3] who, several years later, found 15 per cent of 302 serums positive, males still preponderating, being 23 per cent as compared with 4.7 per cent positive results in females.

Our own experience covers the examination of 1,136 individuals. Each serum was tested with two strains of *B. typhosus*, one, the culture used in routine Widal tests in many laboratories, known as "Mississippi;" the other was the "Rawlings" strain in common use in the manufacture of vaccine. The serums were tested in serial dilutions to the titre of each serum, starting with 1:40. The results recorded (*Table 1*) are those obtained with the former.

Table 1
RESULTS OF AGGLUTINATION TESTS FOR TYPHOID IN 1,136 NORMAL PERSONS

	No.	Per Cent
Individual serums tested	1136	
Positive serums	263	23
Positive in 1:40 dilution	160	14
Positive in 1:80 dilution	68	6
Positive in 1:160+ dilution	35	3
Highest titre 1:640 (1 serum)		

In the case of 106 serums, or about 40 per cent, of those which agglutinated either strain, the "Mississippi" culture agglutinated to a higher titre than "Rawlings," while only four serums agglutinated the latter in higher dilution. In most instances the difference, however, was only one dilution tube. These results are in agreement with a previous study[4] reported from this laboratory. In a series of 270 serums tested with two strains, 24 positive results (1:40+) were obtained with one and only 11 with the other.

The number of positive serums in this series agrees with that found by Rosher and Fielden.[2] Our high percentage of positive tests cannot, however, be explained by vaccination or a prior attack of clinical typhoid fever. It was possible to investigate these points in the case of 60 positive individuals. Only seven had had typhoid vaccine and a history of typhoid fever was elicited from only 5, leaving 48 persons whose serums contained typhoid agglutinins not due to typhoid vaccination or a known previous attack of the disease. If this group of 60 may be considered a fair sample, these results indicate that only 20 per cent of all positive Widal reactions are the result of clinical typhoid or vaccination, and that in the case of some 20 per cent of the general population, some other cause is operative to stimulate the appearance of typhoid antibodies.

These positive results in the apparent absence of stimulation of the specific antigen may be explained in two ways: (1) the non-specific production of typhoid agglutinins by other infections, as suggested by Gilbert and Coleman[1] in connection with their observations on undulant fever patients; (2) subclinical infections with *B. typhosus*. If the latter is the correct interpretation, such a group of persons should yield a higher percentage of typhoid carriers than a group of persons with negative agglutination tests. The examination of these individuals for

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*From Laboratories of Alabama State Board of Health.

healthy carriers is in progress and it is hoped that this further study will help to throw light on the significance of these findings.

Non-specific stimulation seems unlikely in view of the frequent occurrence. If this is the explanation, the non-specific production of antibodies is a more common phenomenon than is generally believed. The distribution, according to age groups, of 662 members of the series, as shown in *Table 2*, does not throw light on the correct explanation. There is a slightly smaller percentage of positive results in children under ten, but this group was small and the difference is not statistically significant. In the higher ages, the percentage of positive individuals is quite constant in each group.

It is noteworthy that the percentage of positive females exceeds that of the males by about 50 per cent in each age group. It is difficult to explain this difference between the sexes on the basis of any of the theories proposed. It is not reasonable to suppose that females, as a group, are exposed to any infection to a greater extent than males and yet the consistently larger number of positive females (about 50 per cent excess in each group) throughout all ages must be due to some other cause than mere chance.

The results of this series of examinations throw further doubt on the diagnostic value of the Widal reaction, at least in a region where typhoid fever has been endemic. It is apparent that little significance can be attached to a positive result, even though vaccination and a prior attack of the disease are excluded. A test which is positive in more than 20 per cent of apparently normal persons is difficult to interpret in the case of any particular individual. The difference in agglutinability between different strains of *B. typhosus* is another consideration which must be borne in mind in connection with the interpretation of results. It is possible for a serum to be positive with one antigen and negative with another less readily agglutinable culture.

Table 2

SHOWING 662 PERSONS GROUPED BY AGE, SEX AND TITRE OF SERUM

Age	Sex	Titre 40	80	160	320	Total
0- 9	M	2.9	0	2.9	0	5.8
	F	4.0	4.0	0	0	8.0
10-19	M	19.4	4.1	0	1.4	24.9
	F	22.2	9.7	1.4	1.4	34.7
20-29	M	10.0	5.0	0	0	15.0
	F	15.3	4.7	1.2	1.2	22.4
30+	M	12.3	3.4	2.7	0	18.4
	F	20.0	5.6	0	1.4	27.0

Figures indicate percentage positive in each group.

It would be interesting to compare our results, obtained in an area of high typhoid prevalence, with similar observations in a locality where the disease is less common. Gilbert and Coleman's[1] series of 150 cases of undulant fever, while not, in every respect, a normal group, yielded results similar to ours, in that definite agglutination occurred in 24, or 16 per cent. These persons were from a population group where typhoid fever, for years, has had a low rate, thus indicating that the occurrence of typhoid infection bears little relation to the production of typhoid agglutinins. The conclusion, consequently, seems inescapable that non-specific production of antibodies occurs and, in the case of typhoid agglutinins, with a considerable degree of regularity. Whether such non-specific stimulation is the result of infection with certain bacteria or is due to some other mechanism, still remains to be determined.

SUMMARY

Agglutination tests for *B. typhosus* with the serums of 1,136 supposedly normal persons yielded 23 per cent positive results.

The past history of 60 of the positive individuals was ascertained; only 7 had had typhoid vaccine and only 5 a clinical attack of the disease, leaving the origin of the typhoid agglutinins unexplained in the case of 48, or 80 per cent. Possible causes for their presence in these serums are discussed.

In each age group positive results in females exceeded by 50 per cent those among males.

The large percentage of positive reactions in a normal population further obscures the diagnostic value of the Widal test.

REFERENCES

1. For references on non-specific stimulation of agglutinins see Gilbert, Ruth, and M. B. Coleman: Agglutination of Typhoid Bacilli in Serums of Patients Having Unrelated Infections. Jour. Infec. Dis., 46: 311, 1930.
2. Lancet, 1:1088, 1922.
3. Jour. Hyg., 30:55, 1930.
4. Havens, L. C.: Jour. Infec. Dis., 43:385, 1928.

DISCUSSION (*Abstract*)

Mr. R. L. Laybourn, Jefferson City, Mo.—I shall open my remarks with the old platitude which we laboratory workers are continually repeating, that the laboratory report does not in itself constitute a diagnosis. The physician alone makes the diagnosis by viewing the history, clinical picture and laboratory findings in the light of his technical knowledge and experience. The laboratory is an instrument of precision and when used by the physician in the same man-

ner and with the same end in view as in the employment of other precision instruments, the stethoscope for example, the laboratory will be of inestimable value to him. The physician who bases his diagnosis entirely on the laboratory findings errs as greatly as the one who does not use the laboratory at all.

In the past, the Widal reaction has been considered quite specific, but recent experience connected with our studies on undulant fever and tularemia have shown that this is not always the case. My attention was called to this fact by a laboratory oversight. We were running parallel undulant fever agglutinations on all microscopic Widal specimens in an attempt to collect some information on the incidence of undulant fever in the State, and through an oversight, a specimen of blood from an aborting cow, which was owned by one of the State institutions, was set up for agglutination against both *B. typhosus* and *B. abortus*. Imagine our astonishment when we found that these microscopic tests showed agglutination with both *B. abortus* and *B. typhosus*. Six specimens from cattle known to be infected with *Brucella abortus* were then collected and checked with macroscopic agglutinations and four of them agglutinated the typhoid bacillus in the lower dilutions, the *B. abortus* agglutinations going much higher than the typhoid in these cases. Agglutinations against *Brucella abortus* are now run parallel on all specimens in my laboratory and there is little doubt that many cases of undulant fever have been called typhoid fever in the past solely upon the results obtained with a microscopic Widal in which the phenomenon of cross agglutination was present. We have found a number of microscopic specimens from human cases which have given agglutinations against both *B. typhosus* and *B. abortus*. Macroscopic agglutinations and clinical histories have proven most of these to be cases of undulant fever.

My personal reaction to Dr. Havens' report is that many of the agglutinations which he has obtained are non-specific, but this opinion can only be proven by carrying out agglutinations with other organisms which have been found to give cross agglutinations and by securing extensive clinical histories which may be difficult, or impossible, to obtain in state work.

Dr. K. F. Maxcy, University, Va.—The occurrence of typhoid agglutinins is apt to be exaggerated in the presence of febrile conditions. This is the so-called anamnesic reaction. Very much the same situation is encountered in the diagnosis of typhus fever by the Weil-Felix reaction. Normal bloods agglutinate Proteus X19 fairly frequently up to a dilution of 1:80. Occasionally one is encountered which agglutinates up to 1:160. The observations of Felix in regard to the specificity of agglutinins for the dissociated "O" type obtained from a culture of Proteus X19 has been extremely helpful in distinguishing the true typhus agglutination from the non-specific group agglutination of Proteus bacilli which is sometimes confusing. Felix advocates the same sort of "receptor analysis" for the identification of the specific typhoid agglutinins. This method has not been tried, so far as I know, in this country. Perhaps it would prove valuable in overcoming some of the difficulties in the serological diagnosis of typhoid fever indicated by Dr. Havens' study.

Dr. Havens (closing).—I do not want to create the impression that agglutination tests are of no value whatever. Like every other laboratory examination, they are of value when and if they are intelligently interpreted. The whole subject of antibody stimulation is very interesting for study, particularly from the standpoint of non-specific development of antibodies.

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Birmingham, Alabama

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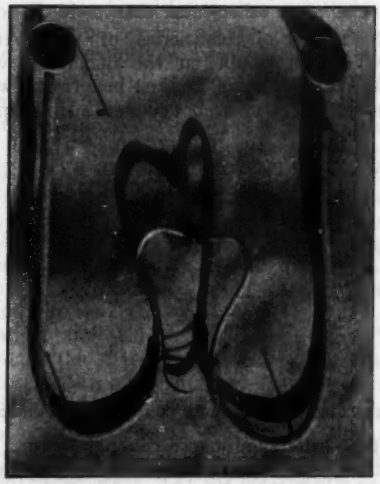

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EDITORIAL DEPARTMENT

SOUTHERN MEDICAL ASSOCIATION
Twenty-Fifth Annual Meeting
New Orleans, Louisiana, November 18-20, 1931

DR. EDWARD H. CARY, PRESIDENT-ELECT, OF THE AMERICAN MEDICAL ASSOCIATION

The American Medical Association, at the Philadelphia meeting, elected, by acclamation, as President-Elect, a former President of the Southern Medical Association, Dr. Edward H. Cary, of Dallas, Texas. It is an honor worthily bestowed upon one who, because of unusual scientific attainments, and distinguished service in organized medicine, deserved such recognition in the greatest medical body in the world.

Dr. Cary, a native son of Alabama, but a resident of Texas during his professional life, has had a remarkable career. Having been Professor of Ophthalmology, Dean, and Dean Emeritus of the Medical Department of Baylor University, he is an outstanding figure in medical education. In the practice of ophthalmology he is recognized as one of the leading physicians of the Southwest; and he is nationally known through his original contributions advancing his specialty. As the founder and owner of the Medical Arts Building in Dallas, the largest and most complete building of its kind in the world, Dr. Cary has proven himself a medical financier and a gifted executive. Likewise in the councils of the Texas State Medical Association, the Southern Medical Association, and the American Medical Association, he has achieved distinction.

DR. EDWARD H. CARY
Dallas, Texas

Had not Dr. Cary been a great physician he would have been a great statesman, or a great financier, or great in any other line of work. The medical profession and mankind are better for his activities in the field of medicine. Dr. Cary's loyalty and devotion to the highest ideals of his profession have endeared him to thousands of confreres in all parts of the country, who rejoice with him in his receiving the greatest elective honor that can come to an American physician.

TOXEMIA OF PREGNANCY

Various workers have reported a lowering of the alkali reserve of the blood in normal pregnancy. This is so constant and early a change that the induction of a slight acidosis following mildly provocative measures has been proposed as an early test for pregnancy. Bulloch,[1] after

1. Bulloch, J. L.: Acetonuria in Pregnancy. Induced Acetonuria as a Test for Pregnancy. Study of 300 Cases. Sou. Med. Jour., 23:560, June, 1930.

examination of three hundred cases, reported correct diagnosis of pregnancy in a very large per cent of them by this method, which consists merely in the observation of acetonuria following ingestion of a meal rich in fats. This is, of course, a much less specific test for pregnancy than the Ashcheim-Zondek or its modifications, but it is very much simpler to perform, and possibly has a degree of accuracy which is clinically quite useful.

Muntwyler, Limbach, Bill, and Myers,[2] of Western Reserve University, have studied the blood chemical changes of women with toxemia of pregnancy, using patients with hypertension of 150-223 mm. of mercury, and with proteinuria. They found that the alkali reserve and total base of these women were reduced, as in normal pregnancy, no more and no less. There was no evidence of accumulation of acid products in the blood. It seemed reasonable to them to believe that the cause of the lowering of the alkali reserve lay in hyperventilation, which they also believe to be its source in normal pregnancy.

Although gravidity is considered a physiological as opposed to a pathological state, many departures from the female normal accompany a so-called normal pregnancy. There are characteristic histological changes in the ureters which make them more rigid, less flexible, and more prone to dilatation.[3] There are general enlargements of the ductless glands, particularly hypertrophy of the thyroid and pituitary. Increased basal metabolism and increased cardiac output are frequently encountered.[4] The normal alkaline reaction of the blood remains constant; there is no accumulation of abnormal acid in the blood, but there is apparently increased excretion of acid products and the circulating fluid contains less alkali for neutralization of toxic acids which may enter the circulation. In pregnancy in general, of course, there is a drainage of the body reserves, mineral and protein. It is possible that the excessive calcium loss to the fetus bears a direct relation to the decreased alkali reserve.

The nutritive requirements of gestation are not supplied in the cases of the majority of gravid women. Knowledge of the metabolic needs of pregnancy has, of course, outstripped application. Although corrective dietary measures and regulation of hygiene, with rest, might largely compensate for the drainage of energy and raw material used in the growth of the fetus, and permit a normal metabolism with a sufficiently positive balance of nitrogen, calcium, iodine, and so forth, and the maintenance of the alkali reserve at a normal figure, ideal conditions are rarely or never approximated. They are still the bright star of the distant future, when the infant and maternal mortality rates are to be zero, and there will be no toxemias of pregnancy. The ideal regimen should begin some months before conception. It is conceivable that fifty years hence women may be required to go into training before pregnancy as before a swimming meet and obtain a medical certificate of fitness before attempting to reproduce.

2. Muntwyler, Edward; Limbach, N.; Bill, A. H.; and Myers, Victor C.: The Acid-base Equilibrium of the Blood in Pathological Conditions. Changes Observed in the Toxemias of Pregnancies. Jour. Biol. Chem., 90:607, Feb., 1931.

3. Hofbauer, J.: Structure and Function of the Ureter During Pregnancy. Jour. Urol., 20:413, Oct., 1928. Editorial, Pyelitis of Pregnancy, Sou. Med Jour., 21: 951, Nov., 1928.

4. Fullerton, C. W.: and Harrop, G. A., Jr.: Cardiac Output in Hyperthyroidism. Bull. Johns Hop. Hosp., 96:203, 1931.

TREATMENT OF HEMOPHILIA

Studies of the clotting of the blood have involved as clever work and as accurate and intricate experiments with unknown reagents as any of the work in immunology; and immunology is the outstanding complexity of modern medical science. The clotting reaction involves a mixture and separation of as many substances as does the Wassermann. Five unknown biological substances have been more or less isolated and analyzed in each instance.

None of the studies of blood clotting has in any way explained hemophilia, a disease which is believed to be confined to the men of the Teutonic race, and carried by their women. The fecundity of females of "bleeder" families is said to be peculiarly great, and among their offspring there is an abnormal predominance of males. This fact would tend to increase the incidence of the disease from generation to generation. The outstanding example of a "bleeder" in Europe today is the oldest son of the former king of Spain, the Prince of the Asturias. A successful and physiological means of combating the tendency to bleed would be rated as one of the world's great medical advances.

A recent investigation by Birch,[1] of the University of Illinois, contains a new departure in

1. Birch, C. L.: Hemophilia. Proc. Soc. Exp. Biol. and Med., 28:752, April, 1931.

the search for the explanation of hemophilia, and describes a method of treatment for which she claims success. She sought the etiological factor, as many others have done, in the blood platelets. The platelets occur in apparently adequate numbers in hemophilia. The usual blood examinations of a "bleeder" are normal in general, except for the anemia from frequent loss of blood.

Healthy red blood cells and platelets maintain their shape in dilutions of salt and water as low as 0.38-0.40 per cent. At lower dilutions of salt, or in distilled water they are laked, or destroyed. For preservation of the normal cell membrane or contour, the osmotic pressure within and without the cell must be nearly equal.

Believing that the platelets of hemophiliacs might be qualitatively different, might be of tougher or frailer fiber than normal, Birch set up platelet fragility tests, according to the common laboratory method for measuring the fragility of red blood cells. The platelets of two severely hemophiliac children were separated from the cells and serum by centrifugalization and measured into graded dilutions of salt. It was found that they were not laked in any of the customary low dilutions of sodium chloride, nor were they crenated at the higher concentrations. The series of dilutions of salt solution tubes was elongated all the way from distilled water to 5 per cent sodium chloride. The platelets of the two bleeders remained whole and normal after twelve hours in distilled water, and showed no crenation until a concentration of 5 per cent saline had been reached. They were thus extremely resistant to variations of osmotic pressure without the cell: both to water which lakes all blood cells and to concentrations of salt far beyond those which crush or crenate the average cell.

Various chemicals which were studied did not reduce the clotting time of the blood of the patients. Physical trauma to the platelets, however, grinding them in a mortar with a pestle for two minutes, was found to alter it. The average coagulation time of the blood of a hemophiliac was ninety-four minutes. Following maceration of the platelets in a mortar, and returning them to the blood, the coagulation time was twelve minutes, or normal. It was apparently the indestructibility of the platelets which caused the prolonged bleeding time in the two cases. The platelets contained the ingredients of the clot, but under ordinary circumstances failed to release them.

Because women carry the disease but are not subject to it, the effect of ovarian extract upon bleeding in hemophilia was investigated. The two high grade hemophiliacs, young boys, were treated with injections of ovarian extract. The kind of ovarian extract is not stated by the author. Both patients were successfully treated and kept free from bleeding phases for about a year in this way. Subsequently, a fresh human ovarian transplant was made into the anterior abdominal wall of one of them. The patient had no hemorrhage at operation and remained symptom-free for five months following the transplant. Ovarian substance thus seemed to be effective in combating the hemophilia of two boys over a prolonged period.

Ovarian extract is possibly harmful in the growth of boys. Various observers[2] have shown that certain extracts retard the development of the testes of male animals. Following frequent injections of theelin and theelol, from follicular fluid, young male animals gain weight less rapidly than their controls, and usually are below normal in the amount of their testicular tissue.

In the case of human bleeders, one wonders what might be the effect of frequent injections of theelin upon such secondary sexual characteristics as the beard, the mental habitus, and the patient's subsequent fertility.

As great success in the control of hemophilia by injections of horse serum and by various tissue juices[3] has been reported. In view of these, the effect of the ovarian extract could be wholly non-specific. Even if the ovarian injections should be found to be more efficacious than other tissue juices in the treatment of a large number of hemophiliacs, it is probable that they should be reserved for extreme cases. The treatment with ovarian extract serves rather to raise a question than to introduce a means of therapy. The studies of the abnormal resistance of the platelets, if this is proven to be a common phenomenon among bleeders, offer a more physiological approach to experiments in treatment.

Dietary measures furnish always the simplest, the most desirable, and probably the least harm-

2. Wade, N. J.; and Doisy, E. A.: Effects of Crystalling Theelol and Theelin and Extracts of Liquor Folliculi on Male Rats. Proc. Soc. Exper. Biol. and Med., 28:714, April, 1931.

3. Cecil, R. L.: Text Book of Medicine, p. 961. Philadelphia: W. B. Saunders Co., 1927.

ful form of therapy of any disease. In scorbutic states, as in hemophilia, there is an abnormal tendency to bleed. Without attempting in any way to relate scurvy and hemophilia, it would seem advisable to give the hemophiliac a strongly antiscorbutic diet.

Book Reviews

The Eye, Ear, Nose and Throat. The Practical Medicine Series. Edited by Charles P. Small, M.D., Albert H. Andrews, M.D., and George E. Shambaugh, M.D. 568 pages with illustrations. Chicago: The Year Book Publishers, 1930. Cloth, $2.50.

The literature in the field of eye, ear, nose and throat during the past year has been reviewed and the outstanding articles incorporated in this volume. Such articles as "The Care of the Eyes in Childhood," "New Researches in the Etiology of Trachoma," and "Some External Eye Diseases of Interest to General Medicine," should be interesting to the practitioner.

Buch and Grove have shown that 19 per cent of cases of otitis media leave some permanent impairment of hearing. The section on mastoiditis and intracranial complications is of particular significance, as in infants the general nutrition is affected.

G. Berberich reviews the advances made in ear, nose and throat disease. Tonsillar ignipuncture as a method of treatment is meeting with greater disapproval. The general man will find this book an aid in diagnosis and treatment, as during the winter months about half his work is in this field.

Southern Medical News

ALABAMA

At the annual meeting of the Medical Association of Alabama in Birmingham in April a recommendation was unanimously adopted for the publication of a state Journal and the first issue will appear in July.

Deaths

Dr. John Daniel Sinkler Davis, Birmingham, aged 72, died May 16 as the result of an automobile accident.

Dr. William Leonard Kimbrough, Linden, aged 72, died April 22 of pneumonia.

Dr. Robert D. Humphries, Vinemont, aged 72, died suddenly March 14.

ARKANSAS

An agreement has been reached by the University of Arkansas School of Medicine and the City of Little Rock for the Medical School to take complete charge of the professional care of all charity patients in the Little Rock General Hospital. By this arrangement members of the faculty of the Medical School will become members of the hospital staff.

Dr. W. A. Snodgrass, Little Rock, has been appointed a member of the State Board of Medical Ex-

Continued on page 34

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Continued from page 658

aminers, succeeding Dr. W. A. Montgomery, Atkins, whose term has expired. Dr. W. W. Verser, Harrisburg, was elected President of the Board, Dr. A. S. Buchanan, Prescott, Vice-President, and Dr. Sam J. Allbright, Searcy, re-elected Secretary-Treasurer. Dr. W. T. Lowe, Pine Bluff, was elected a member of the Credentials Committee.

Deaths

Dr. Robert Howell Taylor Mann, Texarkana, aged 63, died April 17.

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Dr. Shelby A. Turner, Heber Springs, aged 53, died April 10.

Dr. Isaac Ryan, Fort Smith, aged 70, died April 9.

Dr. Julius Kelly Sheppard, El Dorado, aged 57, died suddenly May 12.

DISTRICT OF COLUMBIA

Colonel Robert U. Patterson, Medical Corps, U. S. Army, has been appointed by President Hoover Surgeon General of the Army with rank of Major General, succeeding Major General Merritte W. Ireland, retired.

The Medical Society of the District of Columbia held its annual meeting in May and elected Dr. Arthur C. Christie, President, Dr. James A. Gannon and Dr. Mary O'Malley, Vice-Presidents, and Dr. Coursen B. Conklin (re-elected) Secretary. Dr. John B. Deaver, Philadelphia, and Dr. William Gerry Morgan, President of the American Medical Association, were guest speakers.

Colonel William L. Keller, Medical Corps, U. S. Army, Chief of the Surgical Service, Walter Reed Hospital, received the honorary degree of Doctor of Science at the commencement exercises of the Medical College of Virginia, Richmond.

Washington Medical and Surgical Society has presented Dr. Francis H. Miner and Dr. Paul S. Putzki with fellowships in the Society.

Dr. Elliott P. Joslin, Boston, and Dr. Donald C. Balfour, Rochester, Minnesota, were speakers at a recent meeting of the George Washington University Medical Society.

Dr. C. V. Akin, of the U. S. Public Health Service, has been transferred to Washington from Columbia, South Carolina.

Deaths

Dr. Frederick William Elvrey, Washington, Major, U. S. Army, retired, aged 91, died May 5 of influenza and pneumonia.

Dr. Robert Maitland Ellyson, Washington, aged 69, died May 10 of pneumonia.

Dr. Martha C. Burritt, Washington, aged 71, died April 17.

FLORIDA

Dr. J. W. Hodges, a member of the Duval County Medical Society, has moved to Hampton, Virginia.

Dr. H. W. Counts, Jacksonville, has removed his office to the Peninsular Casualty Building.

Dr. E. L. Huggins has moved from Freeport to DeFuniak Springs.

Dr. Jack Halton, Sarasota, has moved his office to the Professional Building.

Dr. Herbert Bryans, Pensacola, was made a Fellow of the American College of Physicians at the last annual meeting of the College in Baltimore.

Ainah Royce is the new Superintendent of the Morton F. Plant Hospital, Clearwater.

Dr. Frank Schubert and Miss Florence O. Fitterer, both of Miami, were married in January.

Dr. George B. Glover, Monticello, and Mrs. Myra A. Taylor were married in February.

Deaths

Dr. Frank H. Braymer, Bradenton, aged 69, died April 9.

Dr. Benjamin Franklin Smart, Miami, aged 42, died April 18.

GEORGIA

The Georgia Urological Association elected the following officers at their meeting in May: Dr. W. F. Reavis, Waycross, President; Dr. Ernest Corn, Macon,

Continued on page 36

Are You Sure About the Condition of Baby's Bones?

A SIMPLE radiographic examination of babies at birth for evidence of an enlarged thymic condition is becoming a routine procedure in obstetrics; this is a safeguard of untold value. But there is another of equal importance . . . the x-ray examination of non-breast fed babies six or eight months after birth.

Dietary deficiencies cause a lowering of calcium assimilation by the bones, resulting in a rachitic skeleton. This situation can develop before there is outward evidence; but minute internal indication cannot escape the x-ray. Early discovery allows the correction of the cause so that health impairment will not occur. X-rays are one of the greatest aids in guarding health . . . *Employ them regularly.*

In radiography of children the extreme sensitivity of Eastman *Ultra-Speed* and *Diaphax* X-ray Films is especially appreciated by the radiologist. It permits very short exposures and practically eliminates the possibility of blurred detail due to movement on the part of the patient.

"Devils, Drugs, and Doctors"

For a quarter hour of stimulating entertainment, tune in on "Devils, Drugs and Doctors" broadcast each Sunday evening at 8 o'clock, New York time, over a coast-to-coast network of the Columbia System. These talks, sponsored by Eastman Kodak Company, are given by Dr. Howard W. Haggard, Associate Professor of Applied Physiology, Yale University.

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Continued from page 34

President-Elect; and Dr. Allen F. Caldwell, Atlanta, Secretary-Treasurer.

The Atlanta Neurological Society has elected Dr. H. M. Bowcock, Atlanta, President; Dr. Albert F. Brawner, Atlanta, Vice-President; and Dr. Richard B. Wilson, Atlanta, Secretary-Treasurer.

Dr. L. G. Neal has moved from Cleveland to Gainesville.

The Georgia State Medical Society has a prize possession in the form of a gavel presented to them by the family of Dr. Crawford W. Long in memory of Dr. Long, Athens, discoverer of ether anesthesia. It is made from a newel post in Dr. Long's home.

Dr. Charles E. Waits, Atlanta, has been honored with a membership in the American Association for the Study of Goiter.

Dr. David M. Wolfe, Augusta, will have charge of the medical care of the Boy Scouts at Lake Lanier, North Carolina, this summer.

Dr. W. R. Houston, Augusta, recently held clinic at the Duke Hospital.

Dr. W. W. Hardman, formerly of Elberton, has been transferred to the staff of the Veterans' Hospital, Lexington, Kentucky.

Dr. Seals L. Whitely, Cedartown, has been elected City Health Officer.

Dr. Allen H. Bunce, Atlanta, was elected President of the Emory University Alumni Association by the Alumni Council.

Dr. Richard Binion and Dr. W. M. Scott, Milledgeville, have recently opened the City Hospital, which they own and have equipped with all modern conveniences.

Members of the Brooks County Medical Society recently cooperated with the State Tuberculosis Sanatorium at Alto by holding chest clinics.

Dr. Charles W. Crane, Augusta, is the newly elected Professor of Hospital Administration of the University Hospital, Augusta.

The National League of Nursing Education held its thirty-seventh annual convention in Atlanta in May.

Cooperative extension courses were held in June for physicians of the State.

Dr. James J. Clark, Atlanta, has moved his offices to the W. W. Orr Doctors Building.

Dr. Lila Morse Bonner and Reverend Patrick Dwight Miller, both of Atlanta, were married March 7.

Dr. John Brunson Cross, Atlanta, and Miss Frances Pilling were married March 12.

Deaths

Dr. Thomas Bryant Bonner, Lavonia, aged 68, died April 10 of cerebral hemorrhage.

Dr. Clarence Eugene Suggs, Barnesville, aged 46, died April 14.

Dr. James Clarence Daniel, Decatur, aged 61, died May 15.

Dr. Millard S. Brown, Fort Valley, aged 65, died May 8.

Dr. A. J. Logan, Plains, aged 84, died May 12.

Dr. William Henry Harison, Augusta, aged 78, died April 27.

Dr. Columbus H. Turner, Conyers, aged 81, died April 29.

KENTUCKY

The Kentucky Hospital Association met in Louisville in May, with Dr. John R. Wathen, Louisville, President, presiding.

Dr. Charles G. Lucas, Louisville, was elected Secretary of the American Gastroenterology Association at their meeting in Atlantic City recently.

Dr. Raymond M. Evans, Dr. Dennis G. Evans, and Dr. Dewey L. Bunting, Louisville, have moved their offices to the Breslin Building.

Deaths

Dr. Alexander McKenney, Owensboro, aged 69, died April 29 of heart disease.

Dr. Thomas S. Bradford, Augusta, aged 82, died May 4.

Dr. Elijah A. Cherry, Bowling Green, aged 68, died April 30 of influenza and complications.

Dr. James Steele Bailey, Sr., Lancaster, aged 89, died March 29.

Dr. Oscar K. Bond, Catlettsburg, aged 49, died February 16.

Dr. Edward M. Stanley, Louisville, aged 62, died April 22 of cerebral hemorrhage.

Dr. Woodruff T. Chandler, Campbellsville, aged 79, died April 26 of pneumonia.

Dr. Stephen L. Reid, Loretto, aged 64, died April 26 of heart disease.

Dr. Robert Fairleigh McDaniel, Louisville, aged 54, died suddenly April 13 of heart disease.

Dr. John W. Meador, Custer, aged 77, died April 8.

Dr. Floyd Wilbur Hancock, Bedford, aged 56, died recently from an operation for appendicitis.

LOUISIANA

Dr. Fayette C. Ewing, Alexandria, has presented a collection of old prints to the Tulane University Medical School. These prints all have a bearing on medicine and the healing art.

Dr. Charles R. Gowen, Shreveport, is building a new tuberculosis sanatorium at Shreveport which will be opened soon.

The Orleans Parish Medical Society had as its guest

Continued on page 38

DUKE HOSPITAL

Durham, N. C.

WARD PATIENTS. Duke University cannot give charity treatment to all who apply, therefore patients whose incomes are less than $15 per week should apply for examinations or for admission to the hospital wards (whether full pay, part pay or free), through their family physicians, to the Duke Public Dispensary (Tel. Durham F-131) on the days and hours listed below. The charge for examinations in the Duke Public Dispensary is $2, exclusive of X-rays and special tests, and the ward rate is $3 per day, if the patient can pay. Welfare departments and churches should assist in the payment for the needy.

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PRIVATE PATIENTS. Patients who can pay the private rates of $5 to $8 per day may at any time, through their family physicians in consultation with any member of the hospital staff, reserve private rooms by telephoning to the admitting office (Durham F-131). Appointments for private examinations and treatment may be made in advance by telephoning to members of the hospital staff.

Every effort is being made to cooperate with the medical profession, and patients are asked to return to the physicians who referred them to the hospital and public dispensary.

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BIRMINGHAM, ALABAMA

Continued from page 36

speaker at a recent meeting Dr. Walter Clarke, Associate General Director of the American Social Hygiene Association, New York.

Dr. Charles L. Chassaignac, for eight years Superintendent of the Eye, Ear, Nose and Throat Hospital, New Orleans, has resigned.

It is reported that Dr. James Birney Guthrie, New Orleans, is to be Professor of the Principles and Practice of Medicine and Head of the Department of Internal Medicine of the new University of Louisiana Medical School, New Orleans, and Dr. Abraham L. Levin, New Orleans, Professor of Gastroenterology in the Department of Internal Medicine.

MARYLAND

Dr. Henry Barton Jacobs, Baltimore, has been honored by the establishing of a room bearing his name in the Welch Library, Johns Hopkins University School of Medicine.

The Bureau of Child Hygiene of the State Department of Health has a Healthmobile touring the State for the examination of babies and children who are ready to enter school.

Deaths

Dr. Isaac Thomas Costen, Pocomoke City, aged 98, died April 1.

Dr. Henry C. Connaway, Hebron, aged 51, died in March.

Dr. Joshua Edward Benson, Baltimore, aged 70, died May 18 of heart disease.

Dr. Edward Vincent Coolahan, Baltimore, aged 47, died April 29 of pneumonia.

MISSISSIPPI

Dr. John C. Culley, Oxford, was elected President-Elect and Dr. James M. Acker, Jr., Aberdeen, Vice-President of the Mississippi State Medical Association at the annual meeting in Jackson in May.

Dr. Walter W. Crawford, Hattiesburg, announces that Dr. Henry Baby, of Montreal, will be associated with the Crawford Clinic as Chief of the Eye, Ear, Nose and Throat Department.

Dr. T. M. Dye, Secretary of the Mississippi State Medical Association, recently called a meeting of the secretaries of all the county societies, at which time a permanent organization was formed, with Dr. J. M. Acker, Jr., Aberdeen, as President and Dr. Leon S. Lippincott, Vicksburg, as Secretary.

Dr. O. W. Roberts has moved from Sturgis to Eupora.

Miss Ann Sanders is the newly elected Superintendent of Nurses of the Natchez Charity Hospital, succeeding Mrs. Jessie Tyer.

The State Board of Medical Examiners held examinations recently for license to practice medicine in Mississippi.

Deaths

Dr. W. S. Weissinger, Hernando, aged 84, died April 15.

Dr. George David Mason, Lumberton, aged 42, died April 26 of pneumonia.

Dr. Daniel W. Coker, Dubbs, aged 66, died in March of cerebral hemorrhage.

Dr. James A. Ashford, Bolton, aged 80, died March 26.

Dr. William Henry Whitaker, Grenada, aged 71, died March 19.

Dr. Galusha Clyde Stone, Saltillo, aged 52, died April 7.

Dr. Joel Meizer Mann, Crowder, aged 48, died May 14.

Dr. James Beaufort Sims, Aberdeen, aged 69, died May 10 of cerebral hemorrhage.

Continued on page 40

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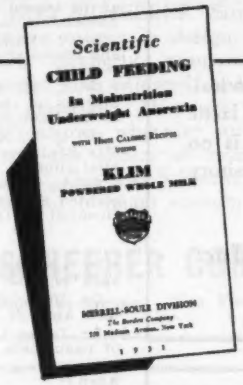

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Continued from page 38

Dr. Samuel M. Jordan, Georgetown, aged 83, died April 19.

MISSOURI

The Medical School of the State University, Columbia, celebrated its second annual observation of Medical Day recently. Dr. Walter E. Dandy, Johns Hopkins University, Baltimore, was the guest speaker.

The American Association for the Study of Goiter held its annual meeting in Kansas City in April.

Washington University School of Medicine, St. Louis, has announced a training course for medical reserve officers for next fall.

Dr. Willard Bartlett, St. Louis, spoke before the Fellows of the Mayo Foundation, Rochester, recently.

Dr. W. McKim Marriott, St. Louis, was a speaker at the annual convention of the Maryland State Dental Association in Baltimore recently.

Dr. J. William Beckman, St. Louis, gave lectures and clinics at Duke Hospital, Durham, North Carolina, recently.

Dr. L. H. Webb has been transferred to Excelsior Springs as the new medical officer in charge of the U. S. Veterans' Hospital.

Dr. Q. U. Newell, St. Louis, addressed the Kansas City Southwest Clinical Society at their monthly hospital clinic.

Bertha Hubacher, St. Joseph, is the newly appointed Superintendent of the new Ransom Memorial Hospital at Ottawa, Kansas.

Deaths

Dr. Leo Christian Huelsmann, formerly of St. Louis, aged 49, died April 25.

Dr. John Walter Kepner, Kansas City, aged 56, died April 29.

Dr. James L. Boone, Sheldon, aged 81, died April 26 of pneumonia.

Dr. Loren Swaney, Kansas City, aged 81, died April 11.

Dr. Louis T. Pim, St. Louis, aged 59, died in May of pneumonia.

Dr. Francis Joseph Sullivan, St. Louis, aged 48, died April 24 of heart disease.

Dr. William A. Coy, Springfield, aged 72, died April 3.

NORTH CAROLINA

Dr. J. M. Northington, Charlotte, was elected President of the Alumni Association of the Medical College of Virginia at a recent meeting.

The new Hugh Chatham Memorial Hospital at Elkin was opened in April with Dr. Harry L. Johnson, Greensboro, Superintendent.

The annual meeting of the North Carolina Hospital Association was held in Durham in May.

Bessie M. Carpenter has been made Superintendent of the Lincoln Hospital at Lincolnton.

Dr. Frederic M. Hanes, Winston-Salem, has been holding clinics on Neurology at Duke Hospital.

Dr. W. C. Davison, Durham, was a speaker at the Nurses' Commencement at Rex Hospital, Raleigh.

Dr. Dan E. Sevier, Asheville, is Director of Public Welfare of that city.

Dr. Frank Coulson Pinkerton, formerly of the University of Virginia Department of Medicine, has located at Pinehurst, and is doing general practice.

Dr. D. E. Ford, New Bern, Health Officer of Craven County, received an invitation to attend the banquet in Washington celebrating the 150th anniversary of the founding of the Red Cross, the invitation coming in recognition of Dr. Ford's distinguished service to the Red Cross in Siberia.

Dr. Julian A. Moore, Asheville, is the newly elected President of the Medical Alumni of the University of North Carolina; Dr. William Coppridge, Durham, is

Continued on page 42

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Continued from page 40

Vice-President; and Dr. L. E. Fields, Chapel Hill, is Secretary-Treasurer.

The Crowell Clinic of Charlotte has added to its staff members Dr. L. D. McPhail, who is in charge of the Department of Proctology.

Dr. Francis Bayard Carter, formerly Professor of Obstetrics, School of Medicine, University of Virginia, is to be Professor of Obstetrics, School of Medicine, Duke University.

The new State Board of Health is composed of the following members: Dr. J. T. Burrus, High Point, President; Dr. J. N. Johnson, Goldsboro; Dr. C. V. Reynolds, Asheville; Dr. H. L. Large, Rocky Mount; Dr. L. B. Evans, Windsor; Dr. S. D. Craig, Winston-Salem; Dr. H. G. Baity, Chapel Hill; Dr. A. T. Goode, Asheville; and Dr. J. M. Parrott, Kinston.

Dr. Charles S. Mangum, Chapel Hill, has completed his thirty-fifth year on the faculty of the University of North Carolina Medical School, where he is now Professor of Anatomy.

Straudie Brown has resigned as Superintendent of Pitman Hospital, Fayetteville.

Dr. George Oren Moss, Cliffside, and Miss Anne Finch were married May 8.

Deaths

Dr. J. Clement Allison, Statesville, died May 13 of pneumonia in Western Pennsylvania Hospital, where he was serving an internship.

Dr. George Dillon Morris, Goldsboro, aged 35, died April 17.

Dr. Herman G. Heilig, Asheville, aged 53, died April 26.

Dr. Horace N. Wells, Murphy, aged 81, died March 10 of pneumonia.

Dr. Henry Byrne Maxwell, Whiteville, aged 58, died March 27 of heart disease.

Dr. William Thomas Holt, McLeansville, aged 77, died April 25 of streptococcic infection.

Dr. Joseph Washington Ring, Elkin, aged 81, died April 14 of angina pectoris.

Dr. Frank Roberts, Marshall, aged 60, died May 3 of heart disease.

Dr. Ralph Sidney Baynes, Hurdle Mills, aged 76, died April 9 of pneumonia.

OKLAHOMA

The Extension Department of the University of Oklahoma and the State Medical Association together are sponsoring post-graduate work for Oklahoma physicians in the nature of a series of clinics.

The Oklahoma City Clinical Society is laying plans for its annual clinical conference to be held in the fall.

The Flower Hospital, Tulsa, has been taken over by Emma and Rose Wiruth.

Deaths

Dr. Bernard Joseph O'Donnell, Tulsa, aged 27, died March 28 at St. John's Hospital, where he was an intern.

SOUTH CAROLINA

Dr. Kenneth M. Lynch, Charleston, recently received the honorary degree of Doctor of Laws from the University of South Carolina.

Dr. J. R. Young, Anderson, is the newly elected President-Elect of the South Carolina State Medical Society, and Dr. E. A. Hines, Seneca, was reelected Secretary-Treasurer.

Marion County Medical Society has elected the following officers for 1931: Dr. J. C. Moore, Jr., Marion, President; Dr. L. S. Miles, Mullins, Vice-President; and Dr. B. M. Montgomery, Marion, Secretary-Treasurer.

The Florence-Darlington Tuberculosis Sanatorium at Florence has for its Superintendent Dr. Eugene C. Hood.

Deaths

Dr. William Simons, Summerville, aged 35, died March 27 of pneumonia.

TENNESSEE

Dr. James F. Brewer, Jr., former tuberculosis clinician for the Tennessee State Department of Health, has been elected Superintendent of the Western Maine Sanatorium at Greenwood Mountain, Maine.

Dr. Eugene B. Elder, Superintendent of the Knoxville General Hospital, has been elected President of the Tennessee Hospital Association.

Dr. Rudolph McCormick, Memphis, has opened offices at 1460 Madison.

Dr. Harvey McLean Williams, Eagleville, and Miss Julia Katherine Bouchard, Nashville, were married recently.

Deaths

Dr. J. H. DeLozier, Newport, aged 63, died March 10.

Dr. Leon L. Sheddan, Fayetteville, aged 64, died April 23 of angina pectoris.

Dr. John T. Sugg, Brentwood, aged 70, died April 29 from injuries sustained in falling from his automobile.

Dr. Ernest Blanton Bowery, Johnson City, aged 42, died April 7 as the result of injuries received in a fall.

Dr. Jacob Herschel Idol, Bean Station, aged 41, died April 12.

TEXAS

The School of Medicine, University of Texas, Galveston, has recently let a contract for the addition to the laboratory building at a cost of $387,000.00, which will double laboratory facilities of the School.

Continued on page 44

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Continued from page 42

Dr. M. W. Sherwood, Temple, is visiting surgical clinics in England, Germany, and France.

Dr. J. M. Ballew, Memphis, is enjoying his first real vacation in forty years of practice, and has gone on a visit to Panama and the Canal Zone.

Deaths

Dr. William Keiller, Galveston, aged 69, died February 22.

Dr. Lee Sloan Payne, Eddy, aged 49, died February 16 of heart disease.

Dr. S. H. Robinson, Melrose, aged 74, died recently of cerebral hemorrhage.

Dr. Edward F. Cooke, Houston, aged 55, died in January.

VIRGINIA

The Southside Virginia Medical Association held its one hundred and tenth quarterly session at South Hill in June.

Dr. Thomas L. Driscoll, Richmond, was recently commissioned a Major in the Medical Reserve Corps of the Army.

Dr. Lawrence T. Royster, University, addressed the Duke University Medical School recently on the occasion of the installation of a chapter of Alpha Omega Alpha.

Dr. W. S. Henning, Richmond, was presented an attendance cup for being the oldest living graduate of the Medical College of Virginia attending the annual alumni dinner.

Dr. Fred J. Wampler, Richmond, will return shortly and take up his duties at the Medical College of Virginia after a leave of absence spent in India.

Dr. Lyndon Frederick Small, University, has gone to Geneva as Acting Technical Expert with the United States delegation to attend a conference on the limitation of the manufacture of narcotic drugs.

The graduating class of the University Hospital School for Nurses, University, held its Commencement Exercises in May. Dr. Kenneth F. Maxcy delivered the address.

Winchester Memorial Hospital at Winchester has re-elected Dr. Hunter H. McGuire President for the thirtieth consecutive term.

Dr. George D. Pettit has located at Chilhowie for general practice after completing his internship at the Johnston Memorial Hospital, Abingdon.

Dr. Carl C. Cooley has been transferred from Norfolk to the Marine Hospital at Ellis Island.

Dr. Charles M. Edwards, Richmond, has been promoted to Lieutenant-Colonel, Medical Reserves, U. S. Army.

Dr. J. Hugh Bailey, formerly of Danville, has located at Scottsburg for general practice.

Dr. Edward C. Joyner has been appointed City Physician of Suffolk.

Dr. John Cecil White, formerly of Richmond, has located in Blackstone, where he will do general practice.

Dr. Joseph H. Smith has located at Farmville where he will practice obstetrics and pediatrics.

Dr. William T. Burch, Alexandria, has been studying in Vienna.

The Virginia Public Health Association has elected Dr. P. M. Chichester, Clarendon, President; Dr. J. J. McCormick, Norfolk, Vice-President; and Dr. A. L. McLean, Courtland, Secretary-Treasurer.

Dr. Howard Lyle Mitchell and Miss Dora Wisborne Witt, both of Lexington, were married recently.

Dr. G. A. L. Kolmer, Salem, and Miss Emma Cameron Cook, Roanoke, were married in April.

Dr. Benjamin Franklin Phillips, Quantico, and Miss Julia Watson Sinclair were married in March.

Dr. Charles Linwood Savage, Sanatorium, and Miss Selma Repass were married in April.

Dr. Donald Snead Daniel and Miss Josephine Townsend Mocre, both of Richmond, were married April 18.

Dr. John Roland Ellison, Jr., and Miss Julianne Butler, both of Suffolk, were married April 18.

Dr. Charles B. Martin and Miss Ruth Davis, both of Danville, were married April 4.

Deaths

Dr. William Wilkinson Murray, Suffolk, aged 86, died April 29.

Dr. Miles B. Jones, Richmond, aged 69, died April 9.

Dr. John Stewart Jamieson, Alexandria, aged 63, died May 18.

Dr. Albert Lee Barrow, Abingdon, aged 53, died March 19.

WEST VIRGINIA

The registration af the annual meeting of the West Virginia State Medical Association was the largest in the history of the Association.

The William and Mary Club of West Virginia has elected Dr. Walter E. Vest, Huntington, President.

Dr. G. L. Straub, Welch, has the general supervision of Grace Hospital since the death of Dr. Charles F. Hicks. Dr. Straub was assistant to Dr. Hicks.

Deaths

Dr. Worthy F. Withers, Arlee, aged 49, died April 4.

Dr. Harry Melville Hall, Wheeling, aged 63, died June 6.

Dr. J. B. Lohan, Charleston, aged 42, died suddenly May 13 of heart disease.

Dr. James Davis, Mullens, aged 33, died May 9.

Dr. W. H. Greene, Weston, aged 53, died May 2.

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